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ARCHIVES OF PEDIATRICS

A MONTHLY DEVOTED TO THE

DISEASES OF INFANTS AND CHILDREN

JOHN FITCH LANDON, M.D., Editor

LEADING ARTICLES IN THIS NUMBER

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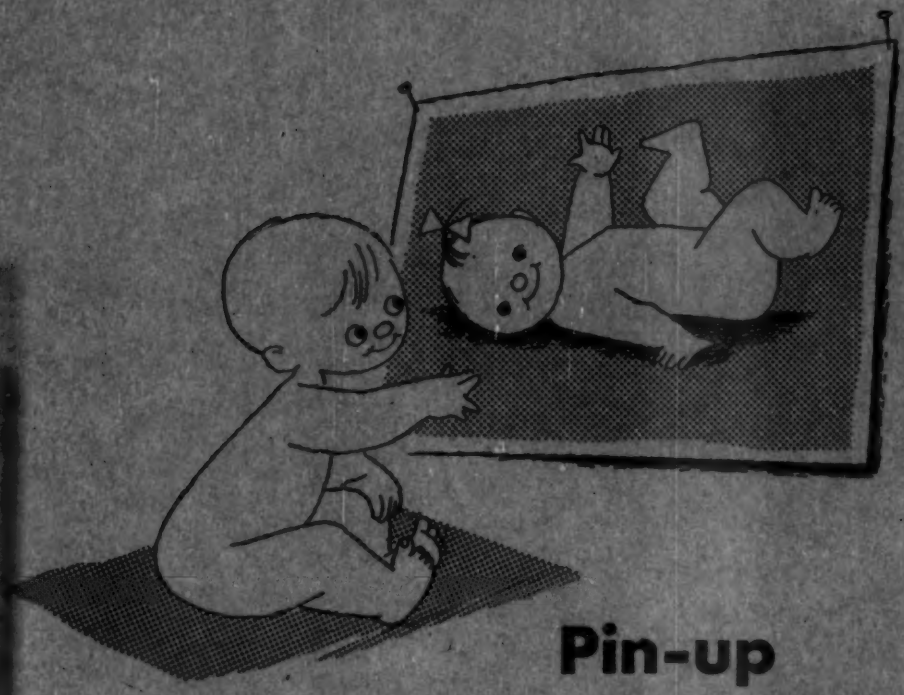

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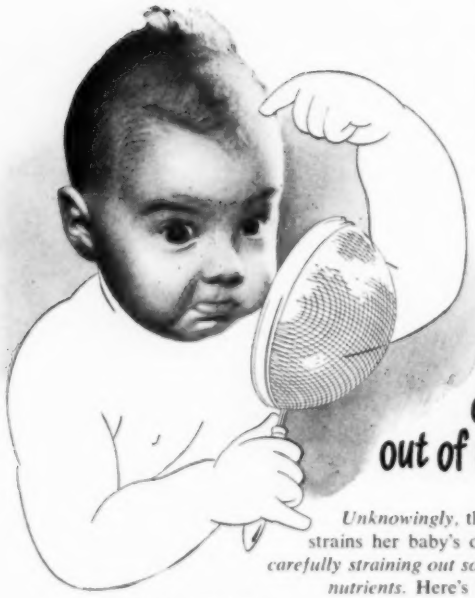

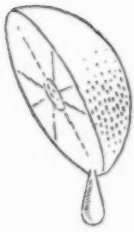

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CLINICAL REVIEW

PEDIATRICS HALF A CENTURY AGO

DEPARTMENT OF ABSTRACTS

ITEMS

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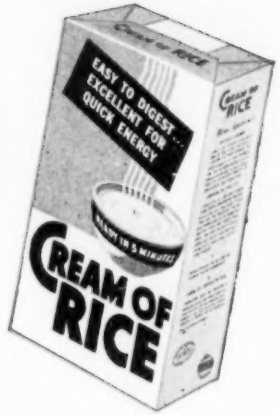

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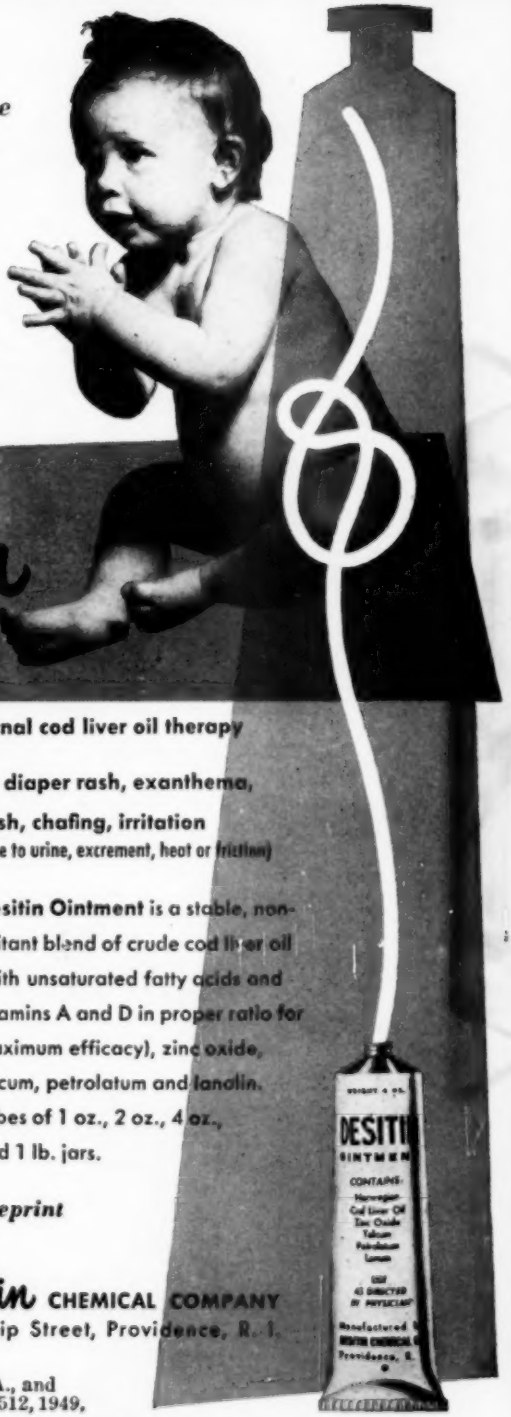

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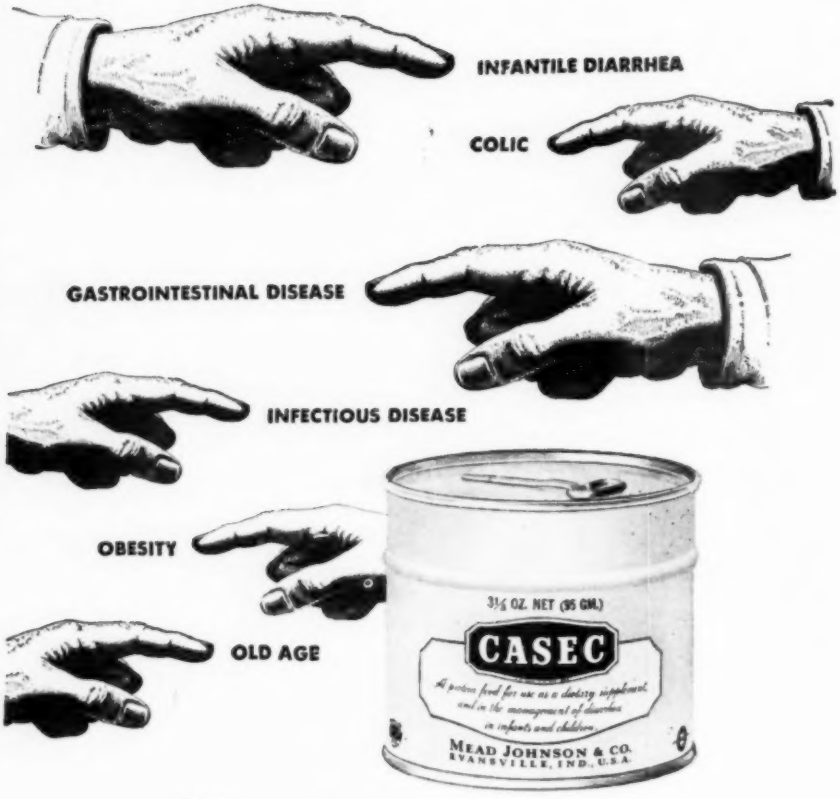

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		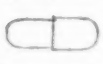		
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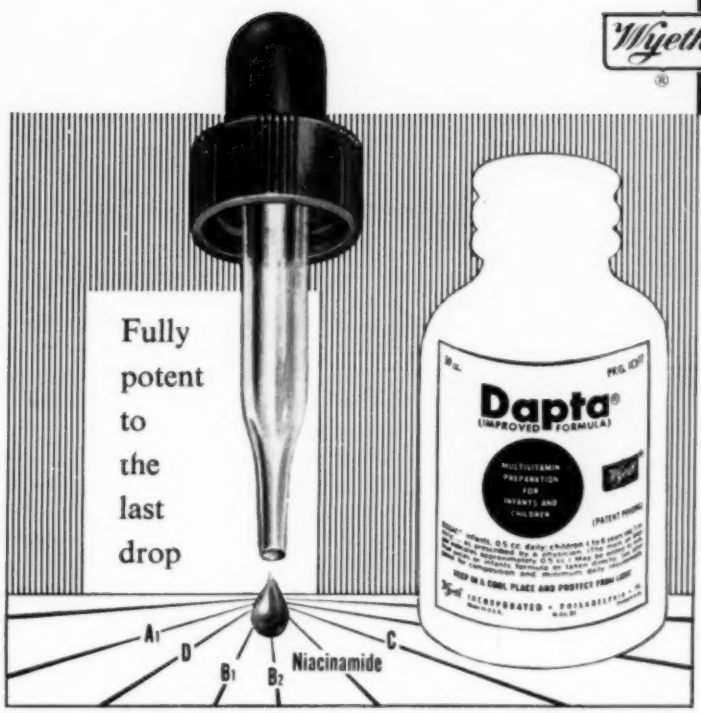

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ARCHIVES OF PEDIATRICS

VOL. 68 JUNE 1951 No. 6

JOHN FITCH LANDON, M.D., Editor

SPONTANEOUS INTRACRANIAL HEMORRHAGE IN CHILDREN*

REPORT OF TWO CASES WITH RECOVERY

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AND

FREDERICK K. SARGENT, M.D.

Urbana, Ill.

Spontaneous intracranial hemorrhage is relatively rare in children and in most instances the cause has been regarded as rupture of an intracranial aneurysm.

The criteria for the diagnosis of ruptured intracranial aneurysm before death was not established until 1923. Symonds,[1] in 1923, reported five cases in which intracranial aneurysm was diagnosed clinically. Cushing[2] stated that the diagnosis of ruptured aneurysm was reasonably certain when subhyaloid retinal hemorrhages and free blood in the cerebrospinal spaces were present following an apoplectic attack or a series of attacks of comparatively sudden onset with symptoms pointing to the region of the internal carotid artery in its intracranial position.

Rosen and Kaufmann[3] reported a case of aneurysm of the circle of Willis, with a symptom-free interval of 27 years between the initial and final rupture. At postmortem examination of the focus of calcification an organized hemorrhage sealing off the initial hemorrhage was noted anterior to the ruptured aneurysm that caused the patient's demise.

Mitchell and August[4] reported a series of 36 cases of aneurysm

* From the Department of Pediatrics, Carle Memorial Hospital and Carle Hospital Clinic, Urbana, Illinois.

observed in 3,080 autopsies. In 16 there was clinical data available and coma had been the presenting symptom in ten. Severe headache was a prominent feature in five and convulsions were noted in four cases. Less frequently observed symptoms were stiff neck (3), hemiplegia (2), dizziness, vomiting, diplopia and a buzzing noise in the head. The latter was noted in a single instance of traumatic arteriovenous aneurysm of the internal carotid artery and the cavernous sinus. In this group there were 26 females and ten males. Of the 36 cases, 20 conformed to the description of the typical "berry" aneurysm, 11 were mycotic, six arteriosclerotic, two syphilitic and one was traumatic.

Martland[5] reported 38 berry aneurysms in a total of 49 cerebral aneurysms, while McDonald and Korb,[8] in an extensive bibliography and analytical study of 572 cases of aneurysm, found 49.5 per cent arteriosclerotic, 32.7 per cent the berry type, 12.2 per cent embolic or mycotic and 5.6 per cent syphilitic.

The actual incidence of intracranial aneurysm may be greater than generally recognized. Alpers[7] reported an incidence of 0.5 to 1.5 per cent in all necropsies. He noted a higher incidence in females than males. These figures correspond roughly to those reported by Michell and August. Mention was made of two cases in which aneurysm failed to be revealed on diodrast study though presence was proven at surgery. It is emphasized that headache associated with ocular palsy may be the warning sign of aneurysm before rupture.

Globus and Globus[8] consider most cerebral aneurysms congenital and not acquired through hypertension or arteriosclerosis. Softening of the brain tissue adjacent to the aneurysm prior to rupture was demonstrated. They called attention to the fact that the anterior communicating and anterior cerebral arteries are the most frequent sites; thus silent brain areas are most frequently affected.

One hundred fifty cases of spontaneous subarachnoid hemorrhage were reviewed by Magee.[9] It was noted that the main incidence of aneurysmal rupture is in childhood or early adult life. No reliable premonitory sign of impending rupture was apparent, but headache associated with ocular palsy is regarded as a significant sign. Fifty-eight patients came to postmortem examination; in 43 there was a ruptured aneurysm. In others, subarachnoid hemorrhage without aneurysm was found. Fifty-six per cent of the cases terminated fatally.

Causes of intracranial hemorrhage other than ruptured aneurysm must be considered in individual cases. These include intracranial injury, encephalitis, parenchymatous cerebral hemorrhage, cerebral venous sinus thrombosis, arteriosclerosis, brain tumor, blast injuries, abscess, syphilis, subdural and extradural hematoma, blood dyscrasia and shock from poisons or drugs, such as insulin and metrazol.

Barlow reported a case with an angiomatous malformation in the middle cerebral distribution with an aneurysmal sac in the center of the tumor mass.[10] This patient suffered 11 attacks between 12 and 26 years of age.

An unusual finding was observed in a case reported by Marie, Mallet, Piat and Ducourneau.[11] This child was brought to the hospital because the father heard an unusual noise, like the cry of a cat, when by chance he placed his ear against the child's head. The child showed no neurological or eye symptoms, and the murmur disappeared after several radiographic examinations. A congenital arterial or arteriovenous vascular tumor was diagnosed.

Wodal and Lowenback[12] presented a case in which the bleeding point during a period of active bleeding was localized by electroencephalography.

The prognosis following rupture of an aneurysm must be guarded. Forrest[13] suggested that the prognosis is more grave with the following: increasing age, presence of cardiovascular disease, hypertension, meningeal signs, leukocytosis (which usually indicates massive or continued bleeding) and the presence of localizing signs. The prognosis is better in the younger age groups, with a history of previous attacks, and in cases where the spinal fluid clears within four to six days.

Sahs and Keil[14] and Schwartz[15] recommended surgery for massive subarachnoid hemorrhage. The latter author reported a case in which the entire medial half of the left frontal lobe of the brain was successfully removed.

CASE REPORTS

Case 1. E. R., male, 16 months of age, was first examined on September 18, 1946. Birth had been normal and birth weight was 7 pounds 12 ounces. He was breast fed and received cod liver oil and orange juice. Immunizations for whooping cough, diph-

theria and tetanus had been administered. Bilateral inguinal herniae and a right internal strabismus were observed during the first few months of life. He sat alone at seven months and stood at 13 months, but had not started to walk at the time of the present illness.

Present Illness. On September 4, 1946, during a carriage ride, he suffered a generalized convulsion which lasted several minutes. Following this irritability and vomiting occurred. In the two weeks prior to examination there was a weight loss of three pounds, but there was no recurrence of convulsions. The only history of trauma obtained had occurred two weeks preceding the convulsion when he had struck his head in a fall out of bed. This had seemed inconsequential.

Physical Examination revealed a 16-month-old male infant, who did not appear acutely ill. Weight was 20 pounds 8 ounces; temperature 99.2° F. (rectal) and blood pressure 110/70. A concomitant convergent strabismus of the right eye was present. Evidence of extraocular palsy was absent and the pupils were equal. Funduscopic examination revealed a large subhyaloid hemorrhage with a typical fluid level flat top, lying temporal to the right disc. The left eye showed similar but less extensive changes. A small amount of blood was present in the vitreous. The optic discs appeared pale, but there was no choking. The heart showed normal rate and rhythm. A faint systolic murmur noted to the left of the sternum in the third and fourth interspaces was not transmitted. The abdomen was negative except for the bilateral inguinal herniae. Deep tendon reflexes were hyperactive and moderate nuchal rigidity was present.

On lumbar puncture a dark red spinal fluid which flowed freely was obtained; protein was 520 mg. per cent and sugar 86 mg. per cent. Spinal fluid cell count showed 31,300 red blood cells and 30 white blood cells of which 85 per cent were polymorphonuclear leukocytes and 15 per cent lymphocytes. Colloidal gold curve was 0000000000. Pandy was positive. Spinal fluid culture was negative and the Kahn was negative. The supernatant fluid after centrifuge was xanthochromic.

Urinalysis showed a specific gravity of 1.016, reaction acid, albumin negative, sugar negative, 1 to 2 red blood cells and 6 to 8 pus cells per high power field. The complete blood count showed

hemoglobin 11.5 grams or 71 per cent, erythrocytes 3,450,000 and leukocytes 10,150 with 18.5 per cent polymorphonuclear leukocytes, 77.5 per cent lymphocytes, 0.5 per cent monocytes, 3 per cent eosinophiles and 0.5 per cent basophiles. Blood platelets were 344,000; bleeding time 1 minute and 10 seconds; clotting time 4 minutes; clot retraction complete within 1 hour. Fragility test showed hemolysis began at 0.46, complete at 0.32; the control showed hemolysis at 0.46, complete at 0.36. Blood serology was negative.

X-ray Examination disclosed a negative skull; the wrists showed three ossification centers and the kidney, ureter and bladder were negative. Roentgenogram of the chest showed increased markings at the right cardiophrenic angle. Several x-ray studies of the skull in November 1946 were negative.

The patient was hospitalized for six days in which period the vomiting stopped; the nuchal rigidity subsided more gradually. At the time of discharge from the hospital, on September 24, 1946, the funduscopic examination was essentially the same as at admission.

He has been followed at intervals for the past four years. The subhyaloid hemorrhages gradually absorbed during a six months' period. On March 7, 1947 there was some pigmentation in both macular areas and the right disc showed primary atrophy.

The last examination was on September 29, 1950, at the age of five years. At that time weight was 40½ pounds and height 43 inches; blood pressure was 100/50 and his general health was good. He had had tonsillectomy and adenoidectomy and the bilateral inguinal herniae had been repaired. Glasses were prescribed in August 1948, and the mother thought vision was improved with them. Strabismus was still present and, if the left eye was covered, vision was poor and he would stumble and fall. Funduscopic examination disclosed a pale right disc; the left disc was of good color but a single small patch of choroidal atrophy was observed. The child appeared to be retarded mentally; however, he was able to play and got along well with his playmates. There had been no recurrence of convulsions.

Case 2. D. R., white male, 6 years of age, was admitted to Carle Memorial Hospital on July 9, 1950. Previous history was negative except for occasional mild earache, occasional vague com-

plaints of abdominal pain and a hemangioma of the left shoulder which had been present since birth.

Present History dated from approximately two hours prior to admission. At that time the patient was riding on a tractor with his father. He suddenly complained of a severe headache; his father lifted him out of the tractor and laid him on the ground. There was no episode of trauma. In a moment he became unconscious following several mild convulsive motions. It had been noted that in the two hours preceding hospitalization he moved his right arm and leg but not the left extremities.

Physical Examination revealed a pale, unconscious boy. Rectal temperature was 99° F., pulse was 84 and strong and regular and the blood pressure was 110/60. The respirations were even and deep, and he gagged occasionally. Movement was noted in the right extremities but not the left. The right pupil was smaller than the left; both pupils reacted to light. Funduscopic examination revealed many retinal and some deep hemorrhages in, on and around the right disc. There were no hemorrhages of the left eye and no papilledema of either eye. A mild left facial weakness was present. The heart, lungs, ears, nose and throat were all negative; the abdomen was soft. There was 2 plus nuchal rigidity, all superficial and deep reflexes were absent, Babinski reflexes were positive bilaterally, and the right leg was stiff on straight leg raising. A slightly raised hemangioma was present on the left shoulder.

Two spinal punctures were performed; and grossly bloody spinal fluid under normal pressure was obtained with both. Examination of the fluid revealed protein 650 mg. per cent, 12 lymphocytes, 200 polymorphonuclear leukocytes and a full field of red blood cells.

Urinalysis showed specific gravity of 1.047, acid reaction, albumin negative, sugar 4 plus and microscopic examination showed 4 to 8 white blood cells per high power field. The complete blood count revealed hemoglobin of 10.0 grams, erythrocytes 3,520,000, leukocytes 13,000 with 89 per cent polymorphonuclear leukocytes and 11 per cent lymphocytes. The blood sugar was 97 mg. per cent and the platelet count was 200,000.

Fragility test showed initial hemolysis at 0.38 and complete at 0.32; the control showed initial hemolysis at 0.44 and complete at 0.34. X-ray examination of the skull was negative. The prothrombin time was 44 per cent.

Within 24 hours after admission the patient had shown periods of consciousness and asked for water. He was given only one intravenous infusion. On the second day he moved all extremities except left arm; and all reflexes had returned except the left abdominal and left cremasteric. By the third day he recognized his parents, but did not move the left arm. On the fourth day he was cooperative and it was noted that touch and pain sensations were absent over the left lower arm. Also there was definite marked weakness of both the left arm and leg. The patient continued to show rapid marked improvement and on the sixteenth hospital day was discharged home. There was residual weakness of the left arm and leg and 1 plus left facial weakness. The reflexes had all returned; those of the left side were all hypoactive and a bilateral positive Babinski reflex persisted.

The patient has since been subjected to air studies and arteriograms which showed a normal ventricular system and no evidence of aneurysm.

DISCUSSION

The paucity of reports of spontaneous intracranial hemorrhage in childhood stimulated this report of two cases. Recovery occurred in both patients with conservative treatment. It is very possible that this condition occurs with greater frequency in childhood than reports in pediatric literature would indicate.

Cardinal clinical findings and symptoms manifested by these two patients were: sudden onset of convulsions in a previously well child, nuchal rigidity, subhyaloid hemorrhages, bloody spinal fluid, headache, changes in pupil size, and the presence of congenital defects. These findings suggest cerebral hemorrhage and on a statistical basis a presumptive diagnosis of ruptured aneurysm could be made.

Arteriograms made in one patient failed to visualize a cerebral aneurysm and the possibility of a cerebral vascular tumor was postulated because of the hemangioma present on the skin. The parents volunteered that in the few weeks preceding the cerebral accident the hemangioma on the shoulder had appeared larger and of darker color. A vascular tumor would be more easily demonstrated by arteriography than an aneurysm in all probability.

The localization of the hemorrhage by neurological examination

presents considerable difficulty. An adequate description of onset is often not available and periods of hours may elapse between the time of onset and detailed neurological examination. Electroencephalography has at times proved of value in localizing the bleeding point.

The immediate treatment after hemorrhage is conservative; however, in certain instances of massive hemorrhage prompt surgery may be indicated. When arteriographic studies are planned they should follow recovery from the acute episode. If a cerebral aneurysm is revealed by this procedure, prophylactic surgery should be considered.

SUMMARY

1. There are numerous causes for spontaneous intracranial hemorrhage, but perhaps the most frequent is rupture of a cerebral aneurysm.

2. The incidence of cerebral aneurysm may be greater than generally realized since certain cases of the condition may be unreported or undiagnosed.

3. Two symptoms suggesting the possibility of aneurysm, prior to rupture, are unequal pupils and ocular palsies.

4. Arteriography, as a diagnostic aid, may provide important assistance to the clinician.

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FOUR NEW FUNGICIDES FOR COCCIDIOIDES IMMITIS*

1. SODIUM CAPRYLATE. 2. ETHYL VANILLATE. 3. FRADICIN. 4. THIOLUTIN.

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Peck and his co-workers,[1] in 1939, first introduced the fatty acids in the treatment of mycotic infections. They theorized and proved that human perspiration serves as a protective coating against infections generally, and fungus infections in particular. The sweat, because of its fatty acid content, was fungicidal and fungistatic, i.e., a physiological antibiotic. Peck and Rosenfeld[2] reported that fatty acids inhibited the growth of pathogenic fungi. Hoffman et al.,[3] of the Ward Baking Company, showed that many fatty acids and their salts were fungistatic. They incorporated sodium propionate, a saturated fatty acid, in bread dough and cake batter to inhibit the growth of molds.

Sodium caprylate, a salt of caprylic acid, having the formula $CH_3 (CH_2)_6COOH$, is a lower saturated fatty acid. Keeney[4] stated that in addition to the value of the fatty acid therapy for fungi it also had an unanticipated antibacterial action too. Theodore[5] found that the lower fatty acids were nontoxic, physiological antibiotics and fungicides, and gave good clinical results in eye infections.

For this study of the action of sodium caprylate on the fungus coccidioides immitis, the R. J. Strasenburgh Company furnished two types of media: Sabouraud's agar and the National Institute of Health formula of serum agar (NIH). Controls from each were used, and the other Petri plates contained 10%, 5%, 1%, ¼%, 1/32%, 1/64%, 1/512% and 1/1024% concentrations of sodium caprylate. The inoculum was single loopfuls from pure coccidioidal abscesses containing pure spherules from known disseminated cases confirmed by the complement fixation test of Dr. Smith from the University of California. The cultures were read daily from the fifth day on. The results of the in vitro studies are seen in Table 1.

*From the Department of Pediatrics and Contagion Division, Kern General Hospital, Bakersfield, Calif.

TABLE 1.

Sabouraud's control	abundant growth
Sabouraud's + 10% sodium caprylate	no growth
Sabouraud's + 5% sodium caprylate	no growth
Sabouraud's + 1% sodium caprylate	no growth
Sabouraud's + 1/4% sodium caprylate	no growth
Sabouraud's + 1/32% sodium caprylate	no growth
Sabouraud's + 1/64% sodium caprylate	no growth
Sabouraud's + 1/512% sodium caprylate	7 colony growth
Sabouraud's + 1/1024% sodium caprylate	7 colony growth
NIH serum agar control	abundant growth
NIH serum agar + 10% sodium caprylate	no growth
NIH serum agar + 5% sodium caprylate	no growth
NIH serum agar + 1% sodium caprylate	no growth
NIH serum agar + 1/4% sodium caprylate	no growth
NIH serum agar + 1/64% sodium caprylate	9 colony growth
NIH serum agar + 1/512% sodium caprylate	no growth
NIH serum agar + 1/1024% sodium caprylate	9 colony growth

The 1/512% concentration represents 19 micrograms per milliliter, and the 1/64% concentration represents 150 micrograms per milliliter with sodium caprylate. The fungicidal concentration lies between the later two concentrations.

TABLE 2.

A-1	Sabouraud's with 1/1024% sodium caprylate
A-2	Sabouraud's with 1/512% sodium caprylate
A-3	Sabouraud's with 1/64% sodium caprylate
A-4	Sabouraud's with 1/32% sodium caprylate
A-5	Sabouraud's with 1/4% sodium caprylate
A-6	Sabouraud's control
B-1	NIH serum with 1/1024% sodium caprylate
B-2	NIH serum with 1/512% sodium caprylate
B-3	NIH serum with 1/64% sodium caprylate
B-4	NIH serum with 1/4% sodium caprylate
B-5	NIH serum CONTROL

In vivo studies on albino rabbits revealed that 50 mgm. per cc. for oral and intravenous uses were compatible for a 2.5 kilogram animal. Postmortem examinations of all organs revealed no deteriorating effects both grossly and microscopically.

Later, in man, intravenous doses of 5 per cent in 5 per cent glucose were given. The highest dosage given was 8 grams in the latter route and even daily intravenous dose of 3 grams in 5 per cent glucose for 3 months. No drug reactions were noted. The human study will be a separate report.

Ethyl vanillate is a new fungicidal drug. It is obtained from wood pulp. Its molecular formula is $C_{10}H_{12}O_4$ (ethyl 4-hydroxy-3 methoxybenzoate. The drug easily undergoes all the chemical reactions characteristic of phenol. It is toxic towards many types of micro-organisms, especially fungi. It has extremely low inhibiting concentrations on: 1. Aerobacter aerogenes. 2. Bacillus mycoides. 3. Aspergillus niger. 4. Penicillium glaucum. 5. Trichoderma species. 6. Metarrhizium glutinosum. 7. Alternaria tenuis.

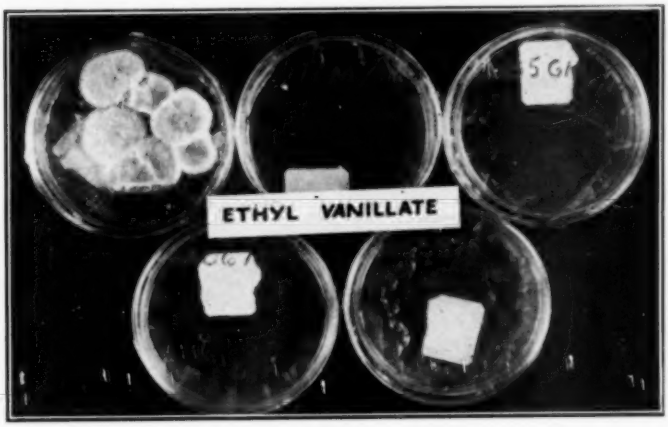

Fig. 1. Top left control with Sabouraud's. Top center: 0.27 Gm. per 100 cc. of ethyl vanillate. 3. 0.135 Gm. per 100 cc. of ethyl vanillate in top right Petri dish. 4. Lower left, 0.0675 Gm. per 100 cc. of ethyl vanillate. 5. 0.03375 Gm. per 100 cc. of ethyl vanillate.

In vitro studies were made on Sabouraud's media only. The inoculum was obtained from abscess containing pure coccidioides showing spherules.

The control cultures showed a luxuriant growth of coccidioides immitis while the culture plates diluted with ethyl vanillate in concentrations as low as 0.03375 gram per 100 cc. completely inhibited growth. (See Fig. 1)

Christie[6] has reported some success with ethyl vanillate in cases of disseminated histoplasmosis. At present I am using this drug

orally in doses as high as 45 grams daily in divided doses in disseminated coccidioidial cases. It is too early to evaluate their therapeutic effects and I hope in the near future to give a preliminary report on its use.

Fradicin is another antifungal antibiotic. Swart[7] and collaborators found that streptomyces fradiae under certain oxygen tension and according to the nature of the culture medium produces "factor X." "Factor X" was found to be endowed with two moieties, one of which was antibacterial and the other antifungal. The antifungal fraction was called "fradicin."

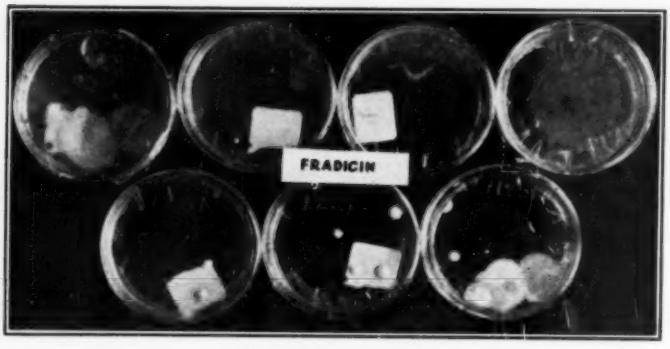

Fig. 2. Control Sabouraud's upper left. 2. Second from upper left; 125 micrograms per milliliter of fradicin. 3. Upper third from left; 62.00 micrograms per milliliter of fradicin. 4. Upper right Petri dish; 31.25 micrograms per milliliter of fradicin. 5. Lower left; 12.5 micrograms per milliliter of fradicin. 6. Lower center; 1.25 micrograms per milliliter of fradicin. 7. Lower right; 0.125 microgram per milliliter of fradicin.

Control in vitro studies using Sabouraud's media revealed luxuriant growth. Plates diluted with fradicin showed complete inhibition at 12.5 micrograms per milliliter in one plate and one small colony in the other. Growth was noted in the higher dilutions of 1.25 micrograms per milliliter and 0.125 micrograms per milliliter. (See Fig. 2)

Hickey[8] stated that mice showed a L.D. $_{50}$ to 4 mg. per kg. in vivo studies. Fradicin is active only in an alkaline medium at pH 7 or above. The ointment is quite irritating at 500 micrograms/g and higher and mildly irritating at about 100 μg/g.

Thiolutin[9], the fourth fungicide reported in this study, is a golden yellow flaxy-like substance which was difficult to get dissolved except by glycerin. Controls on Sabouraud's agar gave luxuriant growth but subsequent higher dilutions of thiolutin showed no growth through 13 micrograms per milliliter and growth at 1.3 and 0.65 micrograms per milliliter. No in vivo studies have been done as yet. (See Fig. 3)

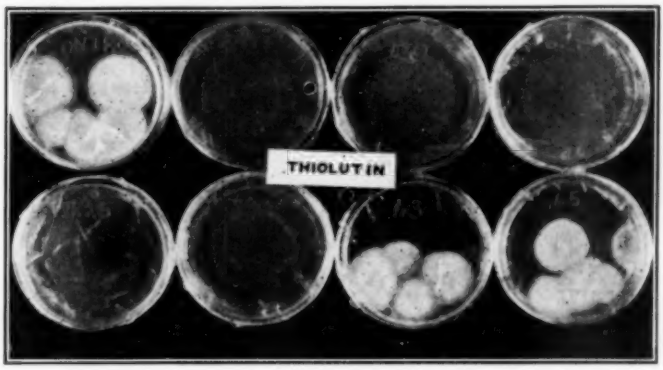

Fig. 3. Upper left;;control with Sabouraud's. 2. Second from upper left; 260 micrograms per milliliter of thiolutin. 3. Third from upper left with 130 micrograms per milliliter of thiolutin. 4. Upper right; Petri dish with 62.5 micrograms per milliliter of thiolutin. 5. Lower left with 31.25 micrograms per milliliter of thiolutin. 6. Second from lower left with 13.0 micrograms per milliliter of thiolutin. 7. Third from lower left with 1.3 micrograms per milliliter of thiolutin. 8. Lower right with 0.65 microgram per milliliter of thiolutin.

DISCUSSION

I feel that we are rapidly approaching finding a fungicide which will be effective in disseminated cases of coccidioides. It is a truism that what is effective in vitro is not necessarily effective in vivo. Actidione[10] is a good example of too high toxicity in spite of some dramatic encouraging clinical results. Extract of buttercup, Protoaneumonin, an excellent fungicide for coccidioides was shown by Conan et al.[11] to be of no value in disseminated coccidioidal infection because it was too toxic. Perhaps a rotation of or a combination of all the various fungicides may be the answer.

I have experienced that ointments of actidione and also sodium caprylate have been effective on local sinuses harboring coccidioidal spherules. Persistent trials of new antifungal agents will certainly be ultimately successful.

CONCLUSION

Four new antifungal agents are discussed. All are effective in vitro against coccidioides immitis. Two are being given clinical trials but it is too early to draw conclusions.

Personal thanks for this study are extended to Dr. Selman Waksman of Rutgers University, Dr. R. J. Hickey of Commercial Solvents Corp., Dr. J. A. Morrell of R. J. Strasenburgh Co. of Rochester, N. Y., Mr. John E. McKeen, President of Chas. Pfizer & Co., and Dr. Harry F. Lewis, and Dr. Irwin Pearl of the Institute of Paper Chemistry of Appleton, Wis., also Dr. Amos Christie of Vanderbilt University School of Medicine, and lastly Dr. Robert Huntington, pathologist, Kern General Hospital.

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THE ROLE OF RADIATION THERAPY IN PEDIATRICS*

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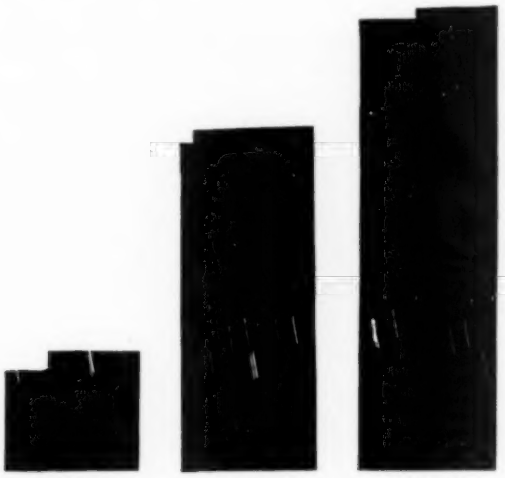
Chicago.

So many physicians have registered surprise at seeing children awaiting treatment in the reception room of the Department of Radiotherapy that we were made aware that the role of radiation therapy in pediatrics was not too generally known. Among many misconceptions about radiotherapy is one that it is the treatment



NUMBER AND DISTRIBUTION OF ALL NEW PATIENTS FOR A 12 MONTH PERIOD.

Fig. 1.

of last resort. Many of our colleagues do not realize that the majority of patients treated with irradiation are treated for non-malignant conditions, and that the scope of radiotherapy reaches beyond the field of malignancy.

To clarify this misconception we reviewed the records of all new patients seen in the Department of Radiotherapy of Michael

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Reese Hospital in a twelve-month period. Of the 1,728 patients so reviewed, 25.2 per cent were children up to fifteen years (Figs. 1 and 2). Of these 436 juvenile patients, 21, or 4.8 per cent, had malignancies (Fig. 3). This percentage may seem unusually high compared to hospital admissions to the pediatric service where the incidence of malignancy usually varies between 0.3-0.5 per cent.[1] This is understandable when we explain that the Department of Radiotherapy functions also as the Tumor Clinic of Michael Reese Hospital and thus serves as a clearing house, so to speak, for malignant cases of the pediatricians on our staff.

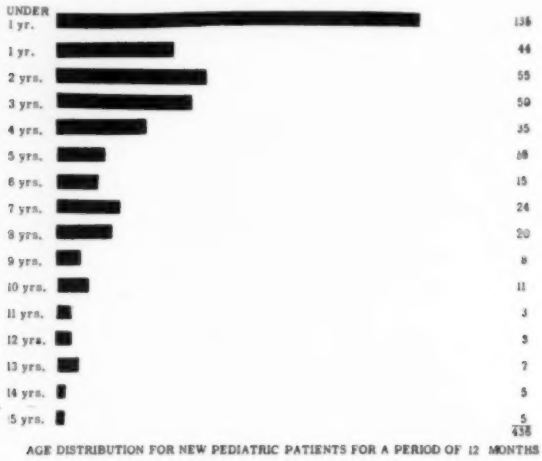
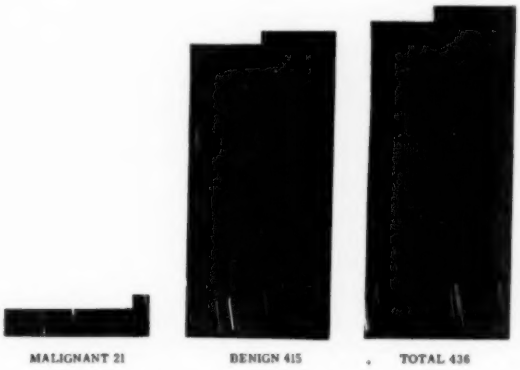


Fig. 2

We have arbitrarily chosen a twelve-month period for review since the purpose of this paper is to demonstrate only the scope of radiation therapy in pediatrics and not to present a statistical analysis of the results of our therapy. A one-year period is sufficiently representative, and although some of the more unusual malignancies might not have been seen during this time, those most commonly reported in the literature were observed with the few exceptions to be discussed later. The frequency of the benign conditions treated remain approximately the same from year to year. This has not always been true. In the early years of our department's

existence, the pediatricians of our staff, too, had to become familiar with the indications for radiation therapy in pediatrics.

Those diseases treated with irradiation fall into four main categories: (1) traumatic or mechanical; (2) inflammatory or infectious; (3) metabolic or endocrine; (4) neoplastic, benign and malignant. This all-inclusive classification might arouse some scepticism, but we believe this can be dispelled when we enlarge on the rationale for radiation therapy and point out the indications or contraindications for its use. Radiation therapy is not always the treatment of preference and it should not be used indiscriminately.



DISTRIBUTION OF BENIGN AND MALIGNANT DISEASE AMONG NEW PEDIATRIC PATIENTS FOR A PERIOD of 12 MONTHS.

Fig. 3.

Each patient as an individual must be studied and evaluated and the proper therapy, medical, surgical, and/or radiation, prescribed after all possibilities have been considered.

The first group of diseases under discussion responding to radiation therapy are those of traumatic origin or due to mechanical irritation. These include strains, sprains and fractures, fibrositis, myositis, bursitis, arthritis, etc. The outstanding symptom of this group is pain, and it is primarily against this symptom that radiation therapy is directed. Very few pediatric patients fall into this group. Strains, sprains and fractures may be frequent but are suc-

cessfully handled by the usual methods of treatment. The remaining diseases are not often observed in the younger age groups. We have used radiation with good results in treating a young boy with myositis calcificans. The symptom of pain was relieved and there was a decrease in the calcium deposits.

Pain is a result of two mechanisms in this group of cases: (1) tension on sensory nerve endings due to the swelling of acute trauma or mechanical irritation as from calcium deposits; and/or (2) lactic acid formation from tissue injury, lowering tissue pH and again acting as irritant to the nerve endings. Irradiation causes vasodilatation with the accompanying increase in the rate and quantity of blood flow through the irradiated area. This increased blood supply hastens the removal of toxic products. Secondly, destruction of the polymorphonuclear leukocytes sensitive to irradiation releases proteolytic enzymes which dissolve dead tissue; thus the lymph and blood vessels are cleared of debris which is removed by the increased blood flow. The initial vasodilatation occurs after about four to six hours and continues for about twenty-four hours. Therefore, because of the increased fluid in the already swollen part, pain may be increased temporarily. This sometimes does occur after the first treatment but rarely subsequently. The similarity of the action of irradiation in trauma to that in infections will be noted. This is not surprising since trauma institutes an inflammatory reaction not unlike infection.

The next group for consideration are those diseases of metabolism, including the endocrine and other secretory glands. These include the functional diseases of the thyroid, parathyroid, pituitary, ovary, adrenals, sweat glands, etc. Here the action is a direct one on the cell. Sufficient radiation is administered to cause cellular change so that a decrease in activity or secretion of glands is accomplished. It is used to good advantage in hyperthyroidism, or hyperparathyroidism, although these occur infrequently in children. We believe it should be used only when surgery is contraindicated and medical management has not proved to be successful. We have treated the lytic skull areas in a case of Hand-Schuller-Christian disease, one of the diseases of metabolic derangement, with complete reossification and relief from pain. Here, too, the action is a direct one on the cell, the irradiation destroying the cholesterol containing reticulum cells permitting replacement by ossification.

Kaplan[2] has written many articles of the value of radiation to the pituitary and ovaries for amenorrhea; we have tried this in adults without success. Furthermore, we feel the lack of menstrual flow in the age group seen by the pediatrician is not an indication for concern or therapy.

The third group of diseases treated with irradiation are those of infectious or of inflammatory origin. The essential rationale of treatment has been discussed under mechanical irritants. Here are included cellulitis, furunculosis, sinusitis, otitis media, thrombophlebitis, pneumonitis, neuritis, gas gangrene, vernal catarrh, and many others. Irradiation is indicated only when the usual methods of therapy have failed to cure or to alleviate the symptoms. We have been able to clear up unresolved pneumonitis, chronic otitis media, tuberculous adenitis and even tuberculous peritonitis with comparatively small amounts of radiation after they no longer showed improvements with chemotherapy. Children with chronic recurring pharyngitis and upper respiratory infections, also eustachian tube deafness, are aided greatly by radiation therapy to the lymphoid tissue in the oral and nasopharynx. Two hundred thirty-one of the four hundred thirty-six patients treated in our twelve-month period were treated for inflammatory conditions; one hundred ninety-three of these received treatment to tonsils and adenoids (ten thymus glands causing obstructive symptoms are included in Fig. 4 under hyperplastic lymphoid tissue and cannot be considered strictly inflammatory); thirty-eight were treated for a variety of diseases, such as cellulitis, otitis media, tuberculous adenitis, sinusitis, etc.

Many of our patients in the group referred for irradiation to the tonsils and adenoids were considered too young for surgery, had allergies, or rheumatic heart disease. Others had had previous surgery with recurrence of symptoms or even of the lymphoid tissue. Some had not had a period free from infection long enough to permit surgery, so that they were referred for temporary relief until surgery could be performed. Many times the relief was of such permanence that surgery no longer was advocated. Uhlmann, Rosenblum, and Perlman[3], in an analysis of four hundred eighty patients so treated in our department, showed complete and permanent relief from symptoms in 25 per cent. Forty-five per cent additional were so improved that they were considered well for all practical purposes. Of these 70 per cent, 20 per cent had previous

tonsillectomies without appreciable benefit. Sixteen and six-tenths per cent showed only temporary improvement, permitting surgery where it was not previously possible. Thirteen and three-tenths per cent were not benefitted in any way by irradiation.

Hyperplastic lymphoid tissue around the eustachian tube results in decreased auditory acuity. This is relieved simply and quickly by irradiation.

A word about thymic enlargement: irradiation is only indicated when it can be demonstrated on roentgenograms that the obstructive symptoms are due to the enlarged thymus compressing the trachea. This is found infrequently when we compare it with the visible thymus seen on routine chest films of infants.

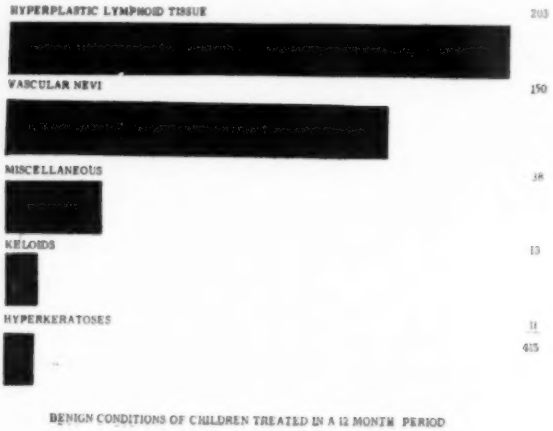


Fig. 4.

Irradiation affects both the hyperplastic lymphoid tissue and combats the chronic or acute infections that usually are the cause of the hyperplasia. As in all infections, the increased circulation aids in mobilizing the body's protective forces. We have already mentioned how the destruction of the polymorphonuclear leukocytes releases proteolytic enzymes which dissolve dead tissues and how the vascular channels are cleared of debris by this combination of proteolysis and increased blood flow. In addition, irradiation produces a general physiochemical effect in the serum that stimulates

increased phagocytosis[4] and brings about the elaboration of an antitoxic factor.[5] Tchaperoff[6] reports the elaboration of para-aminobenozoic acid, a substance important as a bacterial growth factor which is synthesized by tissues in infections but inactivated by irradiation.

The pain concomitant with infection disappears as soon as the tension in the tissues is relieved. If irradiation is given in the first twelve to twenty-four hours of an infection or an inflammatory process, resolution is apt to occur. If given later, it will hasten localization.

The dermatites found in childhood are usually an inflammatory response to fungus, irritation or allergy, and as inflammations are so aided by irradiation when indicated. Some of these are acne vulgaris, eczema, lupus vulgaris, dermophytosis, tinea capitis, favus, etc.

In the last group of diseases to be discussed, those of neoplastic origin, the effect of irradiation is accomplished mainly by the destruction of the tumor cell or by the alteration of the tumor bed with secondary effect on the neoplasm. This group is divided into benign and malignant tumors.

Of the benign neoplastic lesions, in our series, the vascular nevi were by far the most commonly treated. The vast majority of these were seen in infants under one year old. One hundred fifty vascular nevi were treated in the twelve-month period under consideration (Fig. 4). Not all types of vascular nevi respond in the same degree to irradiation; the cavernous hemangioma responds best; the capillary nevus (nevus simplex, flammeus, or port wine stain) responds poorly, if at all. We prefer to wait, if possible, until the child is three months old before treatment, since some of the smaller hemangiomas may regress spontaneously by that time. We have never seen the bulkier, actively enlarging hemangiomas show any sign of regression in a period of observation and usually institute treatment early in these patients. In this group we believe irradiation, especially radium therapy, is the treatment of choice over such methods as injection of sclerosing agents or carbon dioxide snow.

Twenty-four other benign tumors were seen in the period under review; thirteen were grouped together as hyperkeratoses, including warts, both plantar and common; eleven were keloid scars (Fig 4). In the former, irradiation should be used only after

the usual methods of treatment have proved unsatisfactory. In the latter, although it is possible to effectively reduce the size of the scar by direct therapy, we prefer to treat the operative site immediately after the keloid has been surgically removed. This prophylactic type of therapy produces the best cosmetic results.

In the treatment of malignancies, irradiation may be the treatment of choice, as in the blood dyscrasias and lymphoblastomas. It may be used in conjunction with surgery as a preoperative measure

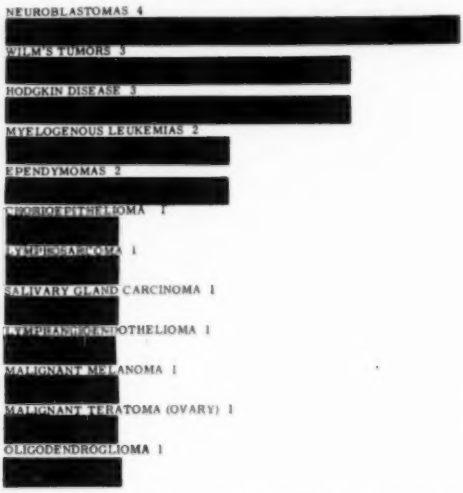


Fig. 5.

to reduce the size of tremendous tumors, such as Wilms' or neuroblastomas, so that surgery may be simplified. It may be used postoperatively following incomplete surgical removal or where statistics show improved final results due to this combined therapy. Irradiation can be directed toward cure or toward palliation. It is used not only to save or to prolong life, but to make what time is left to the patient comfortable and enable the patient to lead as active, as normal, as useful a life as is possible during that time.

Twenty-one malignancies were reviewed in this series (Fig. 5).

Since the interval is short and the actual number of cases small (although we have shown the incidence of malignancy to be relatively high in our series) the distribution of the various types of malignancies may not resemble that in the larger series reported; however, the preponderance of neuroblastomas, Wilms' tumors, brain malignancies and blood dyscrasias is typical. The absence of malignancy of bone and eye, we suggest is just incidental to the short period under observation, since a representative number of Ewing and other bone sarcomas, and retinoblastomas have been treated here over the past twelve years.

It has been slightly more than fifty years since the science of radiation therapy first saw the light of day. Despite one-half century of progress many physicions today remain unaware as to the indication, the contraindications and the modus operandi of irradiation. Many, because of lack of information or by judging the poor results of improper therapy, are prejudiced against all forms of irradiation. Others, at the opposite extreme, consider irradiation as some mystic panacea to which all disease responds. Obviously neither attitude is desirable. The proverbial "happy medium" must be sought to afford the patient the best medical care.

It should be remembered that radiation therapy has a firm scientific foundation and, as in other forms of therapy, it has its indications and its contraindications. It must be administered in such a manner by qualified specialists to achieve maximum improvement without effecting changes, local or general, detrimental to the patient.

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CLINICAL REVIEW

In order to encourage the writing of clinical articles by recent graduates or senior medical students, the ARCHIVES *will publish monthly at least one such paper from the classes of Doctor Reuel A. Benson, New York Medical College, New York, and Doctor Philip Moen Stimson, Cornell Medical School, New York. Other interested medical schools are cordially invited to submit student papers for consideration.*

STILL'S SYNDROME IN JUVENILE RHEUMATOID ARTHRITIS*

ITS CLINICAL ASPECTS WITH A REVIEW OF THE LITERATURE ON THE PECULIARITIES OF THIS SYNDROME

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Rheumatoid arthritis in children has been a subject of increasing interest in the past fifty years. Virchow is known to have mentioned "arthritis deformans" in children and Charcot discussed its relation to rheumatic fever as early as 1881[10,26]. However, it was not until Still[27] published his brilliant paper (1897) on a variant of this disease that widespread attention was focused upon it.

Still[27] described "a form of chronic joint disease in children" which he felt to be entirely separate from rheumatoid arthritis. He assembled 22 cases of arthritic children and concluded that 12 of these were distinct from adult rheumatoid arthritis because of earlier onset, splenomegaly, lymphadenopathy, irregular pyrexia, smaller female preponderance, and the occasional occurrence of pericarditis. Since that time the combination of polyarthritis, splenomegaly and generalized lymphadenopathy in a child has been widely known as "Still's disease."

Angevine[1] and others express the present concept of "Still's disease," namely, that it represents only a variant of rheumatoid arthritis and not a separate disease entity. Schlesinger[25] and other English writers and Coss[8] in this country feel that it is the same as adult with clinical differences based on the age group involved. Because of this, Burdick[4] and others[2] believe that there is no justification for the terminology "Still's disease" and prefer "rheumatoid arthritis, juvenile type." On the other hand, in an extensive

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study of 14 patients with the typical clinical picture, Portis[21] concludes that the clinical course and pathology mark this as "a definite disease entity." Ashmun[2] and also Taussig[28] point out the usefulness of employing the term "Still's disease" to denote this "rather definite" group of cases. Finally, in support of the latter view, Atkinson[3] quotes the finding of a predominance of leukocytes as distinguishing "Still's disease" from "other chronic (lymphocytic) juvenile rheumatism"; Schlesinger[25] feels that the usual Roentgen picture "could almost be described as pathognomonic."

Use of "Still's Syndrome" in This Paper. The controversy over terminology, as presented in the preceding discussion, has led me to coin the term "*Still's syndrome*" in the interests of accuracy. While there is no dissent in the recent literature with regard to the fact that this entity is not entirely distinct from adult rheumatoid arthritis except as modified by age, there is sharp disagreement as to convenient terminology for this quite definite group of cases. The designation Still's syndrome should at least serve to demarcate those cases of rheumatoid arthritis in children with splenomegaly, lymphadenopathy and certain other features from those cases similar to the disease in the adult. At any rate, the nosologic implications of the word "disease" are avoided.

The General Clinical Picture of Still's Syndrome. Little of substance has been added to the classic description of this condition in 1897. Still's syndrome is characterized by a chronic progressive enlargement of joints, usually symmetrical, accompanied by splenomegaly and generalized lymphadenopathy. Still[27] stated that the onset "is always before the first dentition." While this represents the age range of onset in the large majority, Portis[21] noted that while eight of fourteen cases began before age six, six began between six and nine years; Finley[11] and Whitman[31] reported cases in an eleven-year-old and a twelve-year-old, respectively. Still's youngest case was fifteen months old at onset. Atkinson[3], in an extensive review of the foreign literature, found a case in a four-month-old child. (Richdorf's case[23] of polyarthritis in a six-day-old infant proved to be septic, while Lo Presti's[16] fifteen-month-old appeared more like adult-type rheumatoid arthritis).

Still felt that a distinguishing feature of this entity was the smaller relative predominance of females as compared to rheumatoid arthritis. The ratio of females to males in his cases was

1.5:1.[27] In classic juvenile rheumatoid arthritis the ratio was (and is[9]) 5:1 (while the general incidence of rheumatoid arthritis in all ages has been reported as in the ratio 1.5 to 2:1[18]).

The onset is usually insidious. There may be protracted irregular or intermittent fever accompanied by gradual symmetrical enlargement of one or more joints. Limitation of motion and pain on motion is present to a variable degree. While Still was "struck by the absence of pain[27]" in his cases, Atkinson[3], reviewing the literature, found slight pain, increasing on forcible motion, to be typical. Rossdale[24] reports a case with extreme pain, especially on motion. Limitation of motion is due to contractures, followed later by fixation in flexion and muscular atrophy, the electrical reactions remaining intact. Still called particular attention to the typical flexion and ulnar deviation of the wrist[27].

The earliest joints affected are the knees, wrists, and, strikingly, the cervical spine. Later, ankles, elbows and fingers become involved. The temporomandibular and sternoclavicular joints are occasionally affected[21]. The joint enlargement is fusiform, thick, and periarticular. Redness and tenderness are only present in the unusual very acute cases. "Creaking" may be elicited on motion. Although Still stated that there never was any bony grating[27], Schlesinger[25] found grating in shoulder and terminal interphalangeal joints in some cases.

Splenomegaly of significance occurs in almost every case ("definite and considerable" in nine of Still's twelve cases). The enlargement varies from one or two fingers below the costal margin to the level of the iliac crest and roughly parallels the extent of the node enlargement.

A distinctive feature is the lymphadenopathy, which has these important characteristics: (1) Regional nodes of affected joints are primarily and chiefly involved. (2) Size of nodes is directly related to progress of joint disease. Changes in size vary in either direction following febrile or articular exacerbations or remissions. (3) The nodes are firm, discrete, non-tender and freely movable.[3, 25, 27]

Cardiac involvement occurs in a number of cases. Hemic murmurs, due to the anemia, are frequent. Adherent pericarditis, pleuritis and even endocarditis occur. (These will be discussed in detail later).

Anemia is always present, with a tendency to leukocytosis[3, 8, 27]. Hemoglobin may drop to 70 per cent and readings under 50 per cent are not rare.[3] There is an increase in the sedimentation rate and the electrocardiogram usually shows only tachycardia.

Secondary symptomatology may be present. This includes hepatomegaly (35 of 86 cases in Atkinson's series[3]), proptosis (in four of Still's twelve cases) and various erythematous rashes. Profuse sweating characteristically accompanies febrile episodes,[27] although Fitz[12] reports a case with atypically dry skin.

The course is slow with exacerbations and remissions. Recurrences after a maximum period of activity are not often seen[8]. A condition of general joint disease may result. Deaths follow complications.

We shall now pass to the discussion of the more striking features peculiar to Still's syndrome.

Involvement of the Cervical Spine in Still's Syndrome. Involvement of the cervical vertebrae may be said to be characteristic of Still's syndrome. Still called attention to the "very early and almost constant affection of the cervical spine[27]." According to Schlesinger[25] the cervical spine is more often involved in this form of arthritis than in any other. In a thorough study of fourteen autopsies of Still's syndrome (with all other associated and additional diseases ruled out), Portis[21] found affection of the spine in seven, with marked cervical involvement in five. It is interesting to note, by way of contrast, that a fatal case reported by Whitman[31] showed involvement of every joint except the jaw and spine.

Cardiac Involvement in Still's Syndrome. Still[27] considered the occasional presence of adherent pericarditis to be a distinctive feature of this syndrome. There were signs and symptoms of this condition in two of his twelve cases; in autopsies of three others, adhesive pericarditis was unexpectedly found[27]. Of Colver's five autopsies[7], one had "extreme" and another moderate pericardial adhesions. More striking is the series of Portis[21], in which, of fourteen cases, nine had pericardial adhesions and three of the five others showed fibrinous exudate.

Compared to the incidence of pericarditis, endocarditis is found but rarely in Still's syndrome, but has been noted by some investigators. Still[27] himself found some thickening of a mitral valve, but was not particularly impressed by it. Weber[30] found clinical

mitral disease one year after the occurrence of typical Still's syndrome in his patient. Poynton's[22] patient had "obvious valvular disease" eight months after onset. Atkinson[3] quotes cases of two investigators which showed definite endocarditis, and cites ten other writers reporting this.

The Occurrence of Hepatomegaly in Still's Syndrome. Liver enlargement is known to occur as a component of Felty's syndrome in adult rheumatoid arthritis. It may also occur late in the course of Still's syndrome, either as a "secondary symptom" or as a concomitant of a complication. Atkinson[3] reports as a secondary symptom an incidence of 35 in 86 cases reviewed. Poynton[22] reports its occurrence during an exacerbation two years after onset, but it is not clear in this report if the hepatomegaly was actually of cardiac origin. Hepatomegaly accompanied the splenic and lymph node enlargement in Weber's[30] case. Carroll and Nelson[5] and Whitman[31], whose cases developed amyloidosis (to be discussed), each report liver enlargement. In general, one receives the impression that hepatomegaly is of occasional occurrence and is slight in extent, excepting in the presence of amyloidosis.

Amyloid Disease as a Complication of Still's Syndrome. A rarely encountered entity, amyloidosis is a metabolic disease of abnormal endogenous protein metabolism resulting in a diffuse or local deposition of a foreign protein substance, amyloid. It usually is a sequel to chronic suppurative diseases, chronic tuberculosis or multiple myeloma. Rarely, however, and in the absence of these three conditions, amyloidosis may enter as a dread complication of Still's syndrome. Generalized or local (renal, hepatic, splenic) amyloid disease may occur; because of this, albuminuria, which is usually insignificant in the absence of hyperpyrexia in Still's syndrome, should be regarded with suspicion[9]. Marked hepatomegaly should be similarly regarded. Colver[7], Imrie and Aitkenhead[14], Perla and Gross[19], and Coss[8] each report one case. Carroll and Nelson[5] report a case in which the liver weighed 4,300 grams (1/18 the patient's body weight). In none of Still's cases did amyloidosis appear, the earliest reported case being that of Whitman[31] in 1903, in which the liver and spleen were each "three times normal size." Portis[21], reporting on twelve cases in the literature and two of his own, found renal amyloidosis in three resulting in uremic death following the nephrotic syndrome, and

systemic amyloidosis in four others. All of the preceding cases were fatal. The literature records but one case with proved amyloidosis which went on to clinical recovery (Trasoff, Schneeberg and Scarf[29]); this patient had arthritic symptomatology while the amyloid disease regressed (thus, regression of the primary disease was not essential to recovery from amyloidosis!). The Congo Red test was positive, where used, in the foregoing case reports. Finally, it has been held that amyloid disease is a sequel only to "severe or moderately severe arthritis of some duration[29]," and is never found in mild cases.

Iridocyclitis and Band-Shaped Corneal Opacity Complicating Still's Syndrome. A curious complication of Still's syndrome is the extremely rare occurrence of ocular involvement. Holm[13] reports a case of Still's syndrome who developed corneal opacities shortly after onset and one year later exhibited "ribbon-like keratitis" of both eyes. He reports another in which this occurred in one eye and was followed by iridocyclitis and finally the same picture within a year in the other eye. Holm further quotes one such case from the German and two from the Danish literature. Finally, he cites a series of twelve cases with band-shaped corneal opacities, seven of which had a history of arthritic manifestations. Wong[32] collected statistics of twenty-three such cases; he presents one of his own in which iridocyclitis and corneal opacities developed into the typical band-shaped configuration. It is extremely interesting to note that in this latter case the Congo red test was not only strongly positive, but on injection of the dye some of the minute opacities stained faintly pink. With respect to this occurrence, it may also be of interest to note that in three of the cases of amyloid disease complicating Still's syndrome collected by Trasoff et al.[29] iritis was present, and, in two, iridocyclitis. The occurrence of "rheumatic iritis" is mentioned by Parsons and Duke-Elder[17].

Hyperglobulinemia in Still's Syndrome. Both of two papers reporting the level of serum globulin in Still's syndrome stress the hyperglobulinemia in the cases investigated. Taussig[28] reports two patients with an absolute and relative increase in serum globulin, especially the euglobulin fraction. Trasoff et al.[29] report a relative hyperglobulinemia with reversal of the A-G ratio in their case which recovered from amyloidosis.

Occurrence of Eosinophilia in Still's Syndrome. Significant

eosinophilia has been reported in Still's syndrome. The earliest report is that of Whitman[31], in 1903. Coss and Boots[9] describe four patients with an eosinophile count in excess of 5 per cent. The most striking case was Finley's[11] with a 16 per cent eosinophilia.

Skeletal Changes and Residua Due to Still's Syndrome. A striking feature of Still's syndrome is the general arrest in physical development which may occur. The mentality is unaffected[27]. Besides the general bodily underdevelopment, a peculiar bird-like facies has been described[9, 27].

Atkinson[3] has stated that there are no pathognomonic changes. However, Schlesinger[25] and Coss and Boots[9] are in disagreement on this point. Schlesinger drew attention to the presence of what he felt were mixed features of rheumatoid and of osteo-arthritis which may be present, viz., general rarefaction, cartilage destruction, diaphyseal overgrowth, premature ossification and "drilled-out" areas. In a study of 56 cases of juvenile rheumatoid arthritis (not all exhibiting Still's syndrome—splenomegaly in 30 per cent and general adenopathy in 60 per cent) Coss and Boots noted three changes which may occur in these patients: (1) Cervical fusion. (2) Brachydactyly and (3) Brachygnathia (which probably accounts for the "bird-like" facies). Osteophytes and bony lipping are occasionally present[25], although Still felt that they were characteristically absent[27].

Levin[15] points out that, in spite of the general bony decalcification, an intensive chemical study was unable to demonstrate any derangement of calcium balance.

Clinical Amelioration Following Intercurrent Disease. Regression of signs and symptoms of Still's syndrome may follow the intervention of certain disease processes in the patient. Still[27] himself noted marked improvement following measles, scarlet fever and catarrhal jaundice. Fitz[12] presented a case (which at one time had been under Still's care) which improved markedly for one and one-half years following diphtheria. Rossdale[24] also quotes two reports of improvement, one following "enteric fever," and another following diphtheria.

We have previously called attention to the self-limited and remittent character of Still's syndrome. With this in mind, it

becomes very difficult to evaluate any alleged clinical regression as an instance of "post hoc ergo propter hoc."

Prognosis and Prognostic Signs in Still's Syndrome. There is general agreement on the self-limited nature of Still's syndrome[7, 8, 20, 25, 27]. Deaths are due to severe intercurrent disease, e.g., pneumonia[7], or to complications, e.g., amyloidosis. Skeletal residua are more pronounced with a lower age of onset, particularly before the sixth year[27].

Colver[7] studied 69 cases of juvenile rheumatoid arthritis with careful follow-ups. Pickard[20] studied 35 cases, five of which were typical Still's syndrome. The composite results of these studies (reported by Pickard) reveal the following: Complete recovery in 20 per cent, mild or moderately crippled in 14 per cent, severely crippled in 10.7 per cent, and 17.8 per cent were fatal.

Duration of Still's syndrome is variable, usually from two to six years. Of fourteen cases studied by Portis[21], four lasted less than two years, six lasted two to five years, two lasted eight to ten years and one each were observed for twelve and forty-three years, respectively.

The leukocyte count, a most important prognostic sign, has been emphasized by a number of investigators. Coss[8] states that if the usual tendency to slight leukocytosis is replaced by great leukocytosis the prognosis is poor. In the fatal case of Imrie and Aitkenhead[14], the white cell count was 25,800. Coss and Boots[9] observed eight patients with a white count in excess of 25,000; of these, two died, two became worse and four eventually improved.

Remarks on the Differential Diagnosis of Still's Syndrome. It is obvious that those features associated with the arthritis which characterize Still's syndrome, e.g., splenomegaly, adenopathy, rash, widen the scope of differential diagnosis beyond that of simple arthritic states and beyond that of "classic" rheumatoid arthritis. Thus, the following conditions should be ruled out in making the diagnosis: Other arthritides, lymphomas, infectious mononucleosis, tuberculosis, rickets, bacterial endocarditis, meningitis, brucellosis, rheumatic fever, lupus erythematosus, syphilis, and "primary" amyloid disease.

An interesting case is reported from Cuba (Castellanos and Galan[6]) of a six-year-old with fever, polyarthritis, maculo-

erythematous rash, general adenopathy, splenomegaly and uveitis of three years' duration. Still's "disease" was considered the strongest diagnostic possibility. Biopsy, and later autopsy, confirmed the presence of sarcoidosis complicated by tuberculosis.

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PEDIATRICS HALF A CENTURY AGO

From time to time the Archives, which was the first Children's Journal in the English language, will reprint contributions by the pioneers of the specialty over fifty years ago. It is believed that our readers will be interested in reviewing such early pediatric thought.

PERIBRONCHITIS AND INTERSTITIAL PNEUMONIA*

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There are those, like Stoffela, in whose opinion interstitial pneumonia is never primary, or, like Eichhorst, who believe it is mostly secondary. In Jürgensen's opinion interstitial pneumonia is not a clinical, but an anatomical entity.

The father of modern macroscopical pathological anatomy, Rokitansky, claimed that tuberculosis and hyperplasia of connective tissue could originate on a common soil, that is, alongside each other. Heschl reported his observations of its endemic character, finding it rarely in Vienna, frequently in Cracow. Some met it exclusively with other diseases, Buhl with what he described as desquamative pneumonia, and Lebert with croupous pneumonia. Some German-speaking authors, however, like Amberger, have a few cases of a primary diffuse chronic interstitial pneumonia. Eppinger and Wagner declared it to be an occasional independent disease of the lung parenchyma, and Heitler, in a long but interesting paper in the *Vien. Med. Wochenschrift*, Nos. 50, 51 and 52 of 1884, publishes 5 cases of a primary interstitial pneumonia in adults. He calls the condition a parenchymatous pneumonia. He quotes amongst the French, Grisolle and Chomel, who knew of the independent occurrence of interstitial pneumonia. Both, however, describe it to be exceedingly rare. Andral must have seen it more frequently. He makes the positive statement that it need not necessarily develop out of the croupous form, that it may be either local or very extensive, and that while an acute course is observed, it may be chronic and result either

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from an acute affection or run its independent course as a slow process. The modern large manual of Grancher, Marfan and Comby scarcely mentions it.

Amongst the older English writers Corrigan speaks of it as an independent slow inflammation of the pulmonary connective tissue; Stokes knows both an acute induration, and a cirrhotic, grayish, rather anemic sclerosis, and Walshe claims that before cirrhosis can develop, there must be a previous hypertrophy of tissue. (Heitler). Such observations prove the soundness of British medical life. There has been no time in English medicine, in which mere theories and fads could distort the clear sight of English clinicians. Even Brown had to look for enthusiastic support, which he could not find at home, in Germany, France and America.

In the *Traite de Médicine* by Charcot, Bouchard and Brissaud, Vol. IV., p. 471, the scleroses of the lungs are treated by A. B. Marfan. He divides them into the lobar, bronchial or lobular, and pleural varieties. The first includes malaria poisoning, the second dust inhalation, grippe, syphilis and senile changes; the third comprehends those originating in pleural or cardiac diseases. Under a fourth heading he describes what he calls badly defined forms of pulmonary sclerosis. This form, first mentioned by Laennec and Andral, and studied by a number of histologists, consists in an affection of the whole interlobular, interalveolar, and peribronchitic connective tissue. The first stage is a cell infiltration, the second fibrous transformation. This form has often, he says, been taken for tuberculosis in spite of the absence of bacilli and on account of the presence of abundant bloody and serous expectorations. In the few cases carefully studied by Heschl, Eppinger, Marchand and Wagner (13 years, 47 years, 27 years, 47 years) the first days behaved like a genuine pneumonia; but dyspnea and cyanosis led to death. Marfan concludes that these cases also belong to his lobar sclerosis, that means that form which is directly connected with, or derived from, croupous pneumonia.

Our text-books, Tyson, Anders, Osler and others, hardly mention chronic pneumonia except in connection with other forms. In Osler's work diffuse interstitial pneumonia is met with under the following conditions: (1) As a sequence of acute fibrinous pneumonia. (2) As a sequence of chronic bronchopneumonia.

(3) It is pleurogenous. (4) Due to the inhalation of dust. (5) Due to syphilis. (6) Due to compression by aneurism or a new growth, or the irritation of a foreign body in a bronchus. In another part of his book (p. 331 of the fourth edition) he appears to explain the retracted condition of the apices by the presence of tuberculosis only.

In a very able, concise and elaborate article, Winslow Anderson, in the sixth volume of the *Twentieth Century Practice*, treats of the subject of chronic pneumonia, which according to him is synonymous with interstitial pneumonia, cirrhosis of the lung, induration of the lung, pulmonary fibrosis, and fibroid phthisis. Other authors have additional names. His first statement is that it may be local, when it encapsulates morbid deposits and irritating substances, such as tuberculous deposits, hemorrhagic infarctions, abscesses, or foreign bodies; it is more apt to be general, when it depends on croupous or lobular pneumonia or pleuritis. It is always, in his opinion, a secondary disease, and its earlier symptoms are always disguised by the pre-existing affection. It may be suspected when, after a lobar or lobular pneumonia has terminated, the dullness on percussion, bronchial breathing, slight elevation of temperature and cough and dyspnea continue beyond the period at which resolution should have taken place. There is mostly bronchial catarrh and bronchiectasis, ulceration of the bronchial mucous membrane, putrefaction of the secretions, and hectic fever; always cough and pyrexia, sometimes blood in the sputa. Indeed, there is nothing but your fibroid phthisis.

In the supplement to the *Twentieth Century Practice* which appeared two weeks ago—in the language of the trade it is 1903—the same author speaks of chronic pneumonia "as the so-called interstitial or fibroid phthisis." That is why his treatment is, as follows: warm, equally humid climate, no high altitudes, temperature of the room not below 60° F., four meals a day of highly nutritious or predigested food stuffs, olive oil one hour after meals, balsamics for copious expectoration, atropin, dionin and subcutaneous injections of heroin hydrochlorate in 1/24 grain doses. Thereto he adds narcotics and hypnotics, which mean the armamentarium required for those whose only claim is euthanasia.

In his pathologic-anatomical diagnosis of 1900, Orth distinguishes five forms of pneumonia, the fibrinous, the catarrhal,

the purulent (inclusive of the pyemic), the caseous and the productive; all of them have in common the formation of new connective tissue. In the fibrinous variety carnification, as it is here called, is a rare result; in it the alveolar septa are thickened by new formed connective tissue, and by vascular granulation tissue. Both compress the alveoli with its exudate, which undergoes absorption. This process is almost always complicated with pleurisy and bronchitis. Catarrhal pneumonia exhibits a similar process, when the exudate contains much fibrin. Tissue hyperplasia is the result. Caseous inflammation is either a bronchiolitis complicated with fibrous pneumonia; or a true caseous hepatisation with the proliferation of connective tissue cells in the alveolar septa and mainly the intima of the blood vessels. Complication with tuberculosis is not uncommon in this form. Or it is caseous peribronchitis, which is met with in bronchitis and in pneumonia. It is a real new formation of tissue, not the result of inflammation, is found in small deposits and for that reason often taken for tuberculosis. Orth's fifth variety of pneumonia is the productive, that is, cirrhosis. It is found in the cicatrizations around infarctions, new caseous processes, in the shape of peribronchitis, fibrous bronchitis and fibrous pneumonia. The peripheries of these deposits are grey, their centres yellow. In fibrous pneumonia the septa are thickened by connective tissue, they feel and cut like fibrous tissue, there are long grayish septa, the lumina of the alveoli are narrow, their walls sometimes adherent. These indurations are preferably found in and near the apices, and if there be caseous masses nearby, they may heal under the influence of pressure, and lead to the autopsy-findings of calcium or of bone.

In the consideration of interstitial pneumonia we meet with syphilis as one of its main causes in all our literature.

Syphilis of the lung was known four hundred years ago. Paracelsus and Morgagni described it; John Hunter denied and thought he buried it; Ricord and numerous others resuscitated it, and all of us have made its acquaintance. In the young it is more often encountered than in the adult, at least in our era; in hereditary syphilis it is much more frequent than in the acquired, on account of the direct connection in the fetus, through the ductus venosus Arantii, of the umbilical and cava veins. Many of the syphilitic manifestations are known as white pneu-

monia; it is met with in the still-born or those who die soon.

In one or more lobes, sometimes over both lungs, the alveoli are filled with epithelia in fatty degeneration, and the parenchymatous septa are also infiltrated with cells; occasionally there are gummata. But this is not the only change for there is no doubt (Orth) that in white pneumonia there is an interstitial pneumonia as well; and Cornil describes a fibrous change of lymph vessels, with nodes in their walls and caseous degeneration of the endothelium.

Of more import both to the patient and the physician is the exclusively interstitial form of syphilitic pneumonia. There is proliferation of cells, increase of the tissue surrounding the vessels and the bronchi, with subsequent cicatricial shrinking. Gummata are rare in this form, cavities not very infrequent. It is often complicated with the same changes in the pleura. Indeed, many cases appear to originate in the pleura, or in the hilus. Hyperplasia and induration are very marked in this syphilitic form, to such an extent that atrophy of the glands in the mucous membranes, disturbances of the pulmonary circulation and secondary disorders of the heart (hypertrophy and dilatation), are nowhere more frequent. The claim, however, that these heart disorders are a symptom of no other form of interstitial proliferation is untenable. This form is not necessarily fatal, not even at puberty. The puny, undersized and underweight children of from five to eight years that thrive better after a protracted antisyphilitic treatment than after iron and arsenic show frequently the symptoms of interstitial infiltration and retraction.

A nonspecific inflammation, at first rich in cells and succulent, afterwards devoid of cells and retracting and indurating, is met with along the outside of the bronchi, in the blood vessels, in the interlobular and interalveolar connective tissue, with compression and disappearance of the alveoli. There is in the beginning a new formation of capillaries, and an immigration of cells beside those that develop locally. The thickening of the cellular tissue is very often, not always, dependent on pleuritis; in that case there is, in autopsies, a distinct fibrillation extending from the pleura into the lung. Very often, however, the same process begins in the interior, and leaves the pleura intact. The whole process is almost always local, on one side, in one lobe, or in part of a lobe. That

is, mainly when the process is independent. Then it is mostly an apex that is affected, almost always the right, and slowly the disease extends downwards to the neighborhood of the third rib or below. The results are briefly: deficient respiration, retracted lung tissue, deformity of the chest, vicarious emphysema, bronchiectasis with copious secretion, and occasional abscesses, or new connective tissue formations in the shape of firm indurations, or even osseous deposits. But there are many more cases that do not run through the whole course of this degeneration, but remain indolent and innocuous in the stage of retraction and cirrhotic atrophy.

In most of what I have presented to you I have meant to do justice to the observation on the dead. Clinicians, or let us be modest and say practitioners like ourselves, know what they owe to the study of the dead body by ourselves and our masters, Morgagni, Broussais and Rokitansky. But is there an exclusive value in the description of the latest result of a morbid process? Three months or years may have passed since it commenced, suspected first, and closely watched by you in all its varieties of changes, until the dissecting knife took the place of your stetho- and microscope. What can the condition encountered between the last breath and the burial tell then about the first beginning of the process? Its origin and development are under the observation and care of the practising physician. About them he knows more than the pathologist. Moreover, he sees a great many cases that are never seen by the anatomist. In fact, the vast majority of cases of interstitial pneumonia and peribronchitis are such as get well, if not anatomically, still practically, and their owners, when they finally die, are taken off not by the remnants of their interstitial hyperplasia, but by some incidental process. It is particularly in infancy and childhood that this class of hypertrophy of the connective tissue, terminating in shrinking, is most frequently, almost exclusively, observed.

I think I have quoted enough to show the opinions of some of the best authorities. Let me add a single quotation which may be the text for my sermon. In the different editions of my "*Therapeutics of Infancy and Childhood*," and in previous writings, I find what follows: "There are three anatomical varieties of pneumonia in infancy and childhood; the catarrhal or lobular

the fibrinous or lobar, and the interstitial. Nearly two-thirds of the cases belong to the first; nearly one-third to the second, and a limited number to the third class. Not one of them, however, is always found pure and uncomplicated. Indeed, complications of the lobular with the lobar, of either of them with the interstitial, and possibly of each of the three with pleuritis, are quite common. . . . Interstitial pneumonia runs the most protracted course. Fever is liable to be high and prolonged over weeks and months; recovery is rarely complete, induration and retraction of the pulmonary tissue, with bronchiectasis, are quite common."

These remarks are the outcome of clinical observation, extended over dozens of years amongst patients of all ages. What I have opportunities to see weekly is, as follows: An adult, mostly a man, appears with a complaint not connected with his lungs and is examined. Another turns up with a tale of woe. He has been examined by a physician and told that his lungs are affected, and unless he goes to Colorado at once, he must die. They never knew their lungs were affected; they have neither cough nor expectoration; their chests are asymmetrical; there is flattening on one side, depression of an apex, diminished respiration over the corresponding part of a lung, slight or marked bronchophony, slight bronchial expiration, or thoroughly pronounced bronchial respiration, but no râle, no history of a cough, of expectoration or of a lung disease as long as they remember. They are often persons in middle life, sometimes well advanced in years. When other cases are seen in adolescents or those out of their teens, an intellectual mother remembers he or she had a pneumonia, a bronchitis, a lung fever, or a long ill-defined feverish disease, when an infant or young child. Not infrequently the case was a very protracted one, and many fevers would follow one another. In other cases there is no history except that which is indelibly inscribed in their lungs. Adults with the lesions I described are numerous. I feel certain that amongst four thousand office patients, I meet at least fifty such a year. The majority are adults; their history dates back to infancy. Others are children with the same local lesion but a more distinct record. A previous illness is remembered; in many cases the diagnosis was not made.

What I aim at is that these cases should be appreciated at their full but no exorbitant value. While a great many are

the results of a complication of intrathoracic diseases, there are many that run an independent course in the connective tissue either of the bronchial walls or the trabecular or interalveolar septa. There will be plenty of opportunities to verify my experience of a lifetime on the part of those who are not wedded to the thought that the symptoms described by me are invariably due either to tuberculosis or to pleuritis.

SYMPTOMATOLOGY AND DIAGNOSIS

W. V. Leube, in his "Specielle Diagnose der innern Krankheiten," Fifth Edition, Vol. I., p. 138, has the following remarks: "The diagnosis of interstitial pneumonia is almost always of very little clinical importance. It mostly serves only to complete that of other pulmonary diseases. It accompanies the various inflammations of the respiratory organs, chronic bronchitis and pleuritis, the suppurating, gangrenous and caseous processes and neoplasms, and rarely the croupous and catarrhal processes which affect the surface of the alveoli only. A greater importance belongs to interstitial pneumonia when it follows the inhalations of metallic and other dusts and is connected with syphilis."

Now, what I have tried to suggest or to communicate, is the much neglected fact that so-called interstitial pneumonia, or what I should prefer to call it, pulmonary hyperplasia with secondary cirrhosis, is a frequent and frequently independent disease. Moreover, that the full recovery from it, at least as far as the life and comparative health of the patient are concerned, is by no means an uncommon occurrence; that, indeed, a certain measure of pulmonary cirrhosis is not an obstacle to comfort and activity. A few cases of the past few weeks were read, but are not printed with this paper.

The diagnosis of that independent form has its difficulties, less when it appears in its acute than when in its subacute form. Its duration is uncertain; it lasts from a week to months. The temperature is high only in acute attacks; it is mostly moderate, with its morning remissions, rarely with intermissions. An uncomplicated croupous pneumonia undergoes a more or less typical resolution, after six or nine days, rarely after three; the catarrhal pneumonia requires a very much longer time, but its diagnosis—

from its incipiency in bronchitis, its mostly bilateral and posterior location—is generally easier than that of some cases of lobar pneumonia. We all know that the latter is frequently suspected—on account of subjective and objective symptoms—but not proven by auscultation and percussion. Not uncommonly bronchial respiration is not ascertained before the fourth or fifth day. In not a small number of such cases I have noticed that they would run a very slow course, that it would take many weeks before the lungs became normal or nearly so. In many of them you will find that it is the upper lobe that exhibits these symptoms and this course. As I have paid attention to these conditions two score of years, I have met with a great many cases that would finally get well, apparently, but there would remain some dullness and diminished or bronchial respiration. What does that mean? It means that the case was either from the beginning an interstitial pneumonia, or that it was a complication of the croupous and interstitial forms. More! Such cases with retarded diagnosis and retarded—partial—recoveries are the very ones which have the tendency to relapse. When a child has a number of pneumonias in the course of its infancy and childhood, having been apparently well in the intervals, an attentive observer of the well child will mostly find the physical signs of interstitial induration. It is true the complication of the two varieties is one of degrees.

Uncomplicated croupous pneumonia is a surface inflammation. It does not result in induration. There are only few, if there be any, that last months, do not undergo connective tissue hyperplasia and still get well. But it should, on the other hand, be remembered that a recent cell proliferation and fibres that are not quite hardened may undergo absorption, though they be not syphilitic.

The diagnosis from pleuritis may become difficult; that of the latter is not always so easy as those may believe who always look for dullness or flatness, for local pain, for friction sound, and rely on the result of a premature or a timely puncture. Interstitial pneumonia, when independent, is mostly in an upper lobe, pleuritis more frequently over a lower, or all over. When serum or pus make their appearance early, the diagnosis is easy; not to speak of those very bad, but fortunately rare cases in which the diaphragmatic exudation results in compression of the ascending

cava, in congestion and speedy hypertrophy of the liver, and in dropsy of the lower half of the body. The diagnosis of an early complication of pleuritis and interstitial pneumonia may easily be missed at first; later, when the symptoms of pulmonary alteration become more evident, it is again, in interstitial pneumonia, the upper part that is most affected. The diagnosis may sometimes become more difficult on account of the deformities following either; still the flattening of the surface in interstitial pneumonia is mostly referable to the chest wall, that means principally the ribs, while pleuritis is apt to result in atrophy of the muscles of the chest and the shoulder, with or without pain. This difference may mislead, however. But there can be very few cases only, in which, after a long time, the location of the symptoms in the upper (mostly right) lobe in interstitial pneumonia, and of those of pleuritis, friction sound included, mostly over the lower, will not lead to a correct diagnosis.

Tuberculosis is mostly found in the upper lobe, even in the apex, mostly in the right, but there are few cases in which the left is not also infected. Interstitial pneumonia is often found in the upper right lobe only. In the child tuberculosis is apt to spread more generally than in the adult over all the lobes; indeed, its deposits are frequently found in the lower lobes. Tubercular pleurisy spreads soon over the whole pleura of one side. I find it seldom bilateral. Though it be isolated, and not the result of general tuberculosis, it soon gives rise to friction sounds and a very extensive, though not very marked, dullness. Chronic tuberculosis of the lungs is not rarely complicated with laryngitis (less so with enteritis); that is not so with interstitial pneumonia. Tuberculosis is always attended by râles and by cough; in later periods the expectoration does not become fetid. As a rule, interstitial pneumonia is not. I have often been impressed with the suspicion that the observations of apex tuberculosis, not confirmed by the finding of bacilli, were mistaken; that they were in fact local interstitial pneumonias, which finally got practically well, with induration and retraction. Besides, many cases of tuberculosis go hand in hand with an interstitial process and will get well the more readily the more they are connected with interstitial proliferation. Many of you will remember that the action of Koch's tuberculin was believed to consist in the rapid new formation of

connective tissue, which was expected to surround and hide the bacilli, and thus to render them innocuous.

Altogether we may say that capillary bronchitis and lobar pneumonia have their symptoms below and behind, tuberculosis and interstitial pneumonia above, and mostly in front, pleuritis with effusion below and mostly behind, and pleuritis with effusion sometimes, and tubercular pleuritis always, both above and below.

Atelectasis in the infant may persist, rarely by itself, but is usually followed by inflammatory processes, or by emphysema. Two cases of small children, whose asthmatic attacks dated from the earliest infancy, made me connect the latter with the known history of atelectasis of the first weeks after birth. Compression of the lungs by persistent pleural effusion, which is finally absorbed in the same degree in which the flexible chest adapts itself to the smaller compass of the enclosed viscus, we all see. It has its own well-diagnosticated history.

Percussion. Over the retracted apex and indurated lung there is dullness, and more or less resistance to the percussing finger. Induration of the lower lobe allows the diaphragm to ascend. The liver dullness extends above its normal line, and remains stationary during respiration, whenever the lung is tightly adhering to the chest wall. Secondary emphysema and bronchiectasis and the cavities of fibroid phthisis yield their well-known physical signs.

Auscultation. The respiration is vesicular, strongly puerile in the young; in complications with bronchitis there may be râles; for short periods this complication is frequent. It disappears and reappears in acute cases, is seldom met in the chronic. After a while the respiratory murmur becomes feeble, *pari passu* with the development of the connective tissue hyperplasia. When atrophy begins, and sometimes before that time, the respiration, mostly expiration, becomes bronchial. This symptom appears late in subacute or chronic cases, but it lasts, usually forever. It is preceded by bronchophony. There are few râles, or none, in the beginning; none in those instances which remain unchanged, more or less local, and do not degenerate into fibrous phthisis, or are not complicated with emphysema or asthma. Sometimes auscultation, sometimes percussion is more characteristic of the solidification and retraction. In those degenerated cases which are described in all the text-books, râles of every description, the symptoms of

cavities, copious expectoration of serous, mucous, purulent, sanguineous, or fetid sputa become evident. They are well-known, but not observed in the frequent, comparatively mild cases which are the subjects of this communication. Excuse me for again emphasizing that I speak of the latter, very frequent, and often overlooked class.

In a great many of my cases I find the inspiration interrupted, in installments as it were ("saccadée"). This latter symptom belongs by no means to pleural adhesion alone.

Cough. I wish to be emphatic, though my assertion may appear to be overdrawn. There is, in these cases of mine, no cough. Acute cases run rarely without some bronchial irritation, but even in this class there are many that do not cough. When there are rational symptoms and the diagnosis of pneumonia, but little cough, it means interstitial pneumonia. When the case is old, and retraction established again, there is no cough. The authors who speak of cough as a frequent and harassing symptom, or as an early symptom, who describe a dry, or moist cough, and a copious, sanguineous, or fetid expectoration, have seen, or remember, only those cases in which there was an early intense complication in which the latter played the principal part, or the secondary processes of fibrous degeneration.

The Heart and Blood Vessels are affected in proportion to the amount and duration of the induration and retraction. Considerable atrophy of the tissue implies compression and disappearance of capillaries, incompetent circulation, cyanosis, and dilatation and hypertrophy of the right ventricle, with accentuation of the second pulmonary sound. When the upper right lobe is thoroughly affected, the heart may be drawn up and to the right; and the heart and the large blood vessels are more than normally uncovered, and accessible to percussion. That is why the diagnosis of hypertrophy of the heart should be asserted with some mental reservation, exactly as in the cases of rhachitical deformity of the chest, when the flattened side of the narrowed thorax conveys the impression of a hypertrophied heart, merely because it is more extensively in contact with the chest wall. In a similar condition is the heart, when it is drawn to the left by the cirrhotic condition of the left lung. But there are more cases in which cirrhosis, being local, has no such severe result, and the described altera-

tions are but partially developed. The majority of such patients live a fairly comfortable life; they breathe with less than their original lung area, that is all. Fortunately all of us have more than is absolutely required. In all of these cases, even the mildest, the heart sounds are transmitted to a great distance as they are in every form of solidification of the neighboring tissue.

Temperature. It may be high in acute cases, and remain so for weeks; in them bronchial respiration may appear relatively early, and nutrition may suffer quite badly. In most instances high temperatures do not persist long. Week after week, with remissions in the morning, 101° or 102° F., may be reached in the afternoon. These are the cases in which either an infectious fever, such as typhoid or tuberculosis, may be feared, or intestinal autoinfection, with its long duration, occasional erythema, frequent indicanuria, and toxic nephritis may be diagnosticated. The latter is more easily eliminated than the former, i.e., typhoid, in which the recognition of the bacilli is either uncertain or impossible. When the induration is fully established, there is no temperature. I know patients of this kind, who, with all their symptoms of local pulmonary cirrhosis, have not been aware of any disturbance these twenty-five years.

Deformities of the Chest are observed whenever the induration is sufficiently large. They are frequent because the patients are mostly infants and young children with flexible ribs. The apex is retracted, the upper anterior chest flattened. The ribs are close to one another; in Da Costa's experience, who evidently observed adults with complications, the deformity was most often seen over the lower lobes. The vertebræ may be more or less deviating, the scapula of the affected side lower and standing out from the ribs. The circumference of the diseased side is diminished. All this takes place in serious cases. When the upper lobe, the left, or mostly the right, is alone affected, the deformity is accordingly small.

Treatment. The vast majority of cases begin and run their full course in infancy and early childhood. That cannot be repeated too often, for all our text-books refer to adults and to the unfavorable terminations of the disease; and some of the numberless pediatric text-books follow their lead in the most conscientious neglect of observable facts and in treating the young and small as mere miniatures of the old and big. That is why,

if there be preventives, they should be resorted to in infancy and childhood. The best preventive against the diseases of the respiratory organs is protection against infections and against colds; that means strengthening of all the integuments, both mucous and epidermic, and mainly the cutaneous, and thereby the general circulation and its innervation. Good air, plenty of good food. A boy of twelve years should not work in a coal mine at four cents an hour, and the four cents withheld from him and his starving family on account of a debt contracted by his father who was killed in the same coal mine in the employment of the same company, in which we call a Christian country. It is not good for the boy. Perhaps you could convince the employers and the commonwealth of that fact, if more of you doctors would go "into politics." The best means of protecting the child against the influence of sudden exposures and changes of temperature is to get him used to cold water. Begin to wash the well baby when about a year old, after his warm bath, with water of 70, 65, 60 degrees and rub him well until he is dry and thoroughly warm. Diminish that temperature when he is older. Be guided by his strength and weight and previous habits in selecting the treatment. There was a gentleman who lately, before the Association of German Naturalists and Physicians, proved to his satisfaction that exposing children to cold water gives them adenoids and generally poor health. He gives you figures too—60 cases I believe—and figures prove everything to a person who knows how to handle them. In our houses and in our streets, infants and children are more exposed to draughts and the bad influences of infections and of registers, furnaces and sewer manholes than grown up people. Cold draughts creep along the floors of the rooms, just as the dry and by no means unpolluted air of our furnaces, with its smoke and carbonic acid and sulphurous acid, is at the exact height of their noses. It is fortunate, however, that most of the virulent microbes swept into the sewers from dwellings and hospitals find their graves amongst the saprophytes of putrefaction.

The mention of hospitals reminds me of a preventive of a negative nature. Those of you who control babies' hospitals will do well to remove patients, as soon as the recovery from a disease for which they were admitted is accomplished. The communicability of lobar pneumonia from one bed to another is, I hope, an estab-

lished fact; and the frequency of enteritis in every baby ward is a common source of pneumonia. It is true that the latter form, so caused, is almost exclusively lobular. But both the lobar and the lobular variety may give rise to interstitial complication. When this is once started, relapses are frequent, one may say almost certain. Besides, the baby in a hospital cannot have sufficient exercise. It is in its crib or on the floor, with insufficient muscular action and unstimulated circulation. Hypostasis, like ill nutrition, is the result.

Is there a way of fortifying anemic, puny, undersized and underweight infants and children, beyond attending to their hygiene? Their diet should not consist of unmixed and unimproved cow's milk too long. Its tendency to produce dyspeptones and its lack of iron contributes to the development of rickets and of anemia. Animal food and cereals are indispensable.

Medicinally also, we may do a great deal. Our tissue builders are too often neglected. Arsenous acid, a milligram, more or less, daily may be given in small doses after meals, plentifully diluted, for months in succession; phosphorus acts in the same way and never gives rise, when administered medicinally, to any symptoms of poisoning. A baby of a year may take ten drops of the elixir of the pharmacopœia three times a day for three months in succession. Those children of five or seven years who do not thrive on that treatment and on food which contains iron enough, should be suspected of parasyphilis; their fathers' histories should be scanned and not too easily allowed the benefit of any doubt. For these children mercury, with or without iodides or iron, will often accomplish what diet and arsenic and phosphorus were unable to do. Quinin has not satisfied me. In fact dozens of years ago I gave it up in these cases as not fulfilling any rational indication. When the heart muscle is feeble, together with all the rest, those of you who believe in medicines as I do will find that the equivalent of a grain of digitalis given daily, for several months in succession, in refracted doses, will act very favorably on the myocardium of a baby a year old, and by improving circulation will nourish the heart and the rest of the body. Those of you who do not will do well to be converted.

When the disease is acute, subacute, independent or complicated, it requires attention to circulation and nutrition, rarely to tempera-

ture. It has appeared to me that frequent and protracted warm bathing, 95° to 90° F., had a still better effect in this form than in any other. In other respects the dietetic and medicinal treatment is like that which you would employ in other varieties of pneumonia, with one exception. Do not forget that recent cell proliferation and the recently formed connective tissue are absorbable and should be met by treatment. Iodin should be given early; no matter whether you select or are compelled to select, the potassium or sodium salt, iodipin or hydriodic acid. We should not wait too long before beginning that treatment. Organized tissue, unless it be the result of secondary or tertiary syphilis, is no longer influenced by iodids. Treatment should be continued a long time, and may be intermitted and resumed. There may come a time for iodid of iron, when there is anemia and no longer any elevation of temperature.

Chronic dormant cases require gymnastics of the chest muscles but only under the direction of a medical person who knows how to appreciate the possibilities of a strained heart and the danger of relapses. I am yet to see the owner of a professed gymnasium that knows enough or cares enough. I have seen plenty of cases recurring after over zealous gymnastic teaching. A crippled lung must not run in an Olympic race.

As in the cases I speak of—I repeat, the vast majority—there is no cough and no expectoration; there is no indication except the attention to the general health—good food and clothing, cold water, no overwork, outdoor life, and equable climate, for the stronger an altitude of from 1,200 to 2,500 feet, for the feeble the South, the Riviera or Montreux, Cannes, or Tangiers. That is, for those who can afford it. The poor will fare according to the state of civilization and the sense of responsibility prevalent in the commonwealth. Both are low. If the money strenuously squandered by this Republic on wars outside and frauds inside were spent on physical and mental schooling, in city improvements, on sanitation for the tubercular and the weaklings, on the saving of children condemned to subterranean labor, on the rebuilding of our murdered forests, there would be an eternal Christmas on earth, mankind nearer its destination, and this Republic the feast of the old continent's hungry eyes. There would at last be "glory to God in the highest, and on earth peace, and good will toward men." I repeat ladies

and gentlemen, it is time that more of you doctors and particularly you family physicians and pediatrists, should "go into politics."

In some young, in too many of the adult, the further development of peribronchitis and interstitial pneumonia may be that into emphysema, asthma, bronchiectasis, caseous degeneration, abscess, gangrene, cavities, and death. These sad themes are elaborated in our text-books. Your Tyson, Anders, Osler and all the rest have instructive chapters on these subjects. It need not always be death even in what appears to belong to the worst cases. I discharged a few months ago a colored girl of four years that entered the hospital with the history of a long continued interstitial and lobar pneumonia. She was admitted with fever, a big cavity in her right lung, constant cough and copious bloody, and purulent, extremely foul, expectoration. The cavity was at a distance of more than 2 cm. from the chest wall, but so dense was the gray, hard pulmonary tissue, that after a resection of a rib I used the knife, not the cautery, to open the abscess cavity, and lost not more than 4 c.cm of blood during the whole procedure. She was irrigated, treated with arsenic and iodids, and got well, with lung enough left to keep her comfortable under favorable circumstances.

In emphysema and asthma, in spite of the auscultatory difficulties, the differences in the amount of air entering the lungs and the slight changes of the percussion note discernible to a practiced ear, speak of previous interstitial inflammation, thickening or retraction as the case may be. These cases are frequently benefited by iodids, not alone on account of their influence on the heart and blood vessels, but of their powers as absorbents.

GANGRENE AFTER SCARLET FEVER. (Maandschrift voor Kindergeneeskunde, Leyden, 18: 55, 1950). Bethe cites a 5-year-old girl in whom gangrene of both legs developed after an attack of scarlet fever. It was decided to amputate the left leg 8 cm. below the groin. Following the amputation, the general condition of the child improved rapidly and necrotic tissue sloughed off the right leg. The child could be discharged after five months with a temporary prosthesis. The author reviews the literature on the occurrence of gangrene of the extremities after scarlet fever.—*Journal A.M.A.*

DEPARTMENT OF ABSTRACTS

CRUICKSHANK, A. H. AND MITCHELL, G. W., JR.: MYOCARDIAL, HEPATIC AND RENAL DAMAGE RESULTING FROM PARA-AMINOBENZOIC ACID THERAPY. OBSERVATIONS IN HUMAN CASES AND EXPERIMENTAL ANIMALS. (Bulletin Johns Hopkins Hospital, 88:211, March 1951).

Two cases of acute rheumatic fever in girls of 7 years and 10 years of age, and one of arthritis of undetermined origin in a boy of 13 years of age that had received large doses of para-aminobenzoic acid came to autopsy and showed marked to extreme deposits of fat in the epithelial cells of the liver, kidneys and myocardium. These lesions were believed to have been caused by the para-aminobenzoic acid, and this was confirmed by the production of fatty changes in the livers, kidneys and hearts of rabbits to which the drug was administered. The use of large doses of para-aminobenzoic acid in therapy is not without danger.

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GREENSPAN, R.; MACLEAN, H.; MILZER, A, and NECHELES, H,: ANTACIDS AND AUREOMYCIN. (American Journal of Digestive Diseases, 18:35, Jan. 1951).

Thirty milliliter of aluminum hydroxide gel, administered 15 minutes before a single oral dose of aureomycin, markedly depressed the serum aureomycin levels in 10 subjects. The simultaneous use of these two drugs is contraindicated. Thirty milliliter of carmethose given in the same manner had no demonstrable effect on the aureomycin level of the serum, and effectively diminished the gastro-intestinal disturbances frequently occurring with aureomycin therapy. Amphojel adsorbs aureomycin in vitro. It does not destroy or inactivate the latter, but it seems to hold it firmly, not permitting intestinal absorption. Carmethose does not adsorb aureomycin in vitro, and does not interfere with intestinal absorption.

AUTHORS' SUMMARY.

WEINSTEIN, L. AND SHELOKOV, A.: CARDIOVASCULAR MANIFESTATIONS IN ACUTE POLIOMYELITIS. (New England Journal of Medicine, 244:281, Feb. 22, 1951).

Abnormalties of the electrocardiogram occur frequently in

the acute phase of poliomyelitis. Their appearance is associated with the severity of the infection, and not with the age of the patients. Hypertension is relatively common in acute poliomyelitis. Its developument in most cases is probably due to hypoxia; return to the normotensive state can be produced by maintaining adequate ventilation. Acute pulmonary edema is common in fatal cases of the bulbar forms of poliomyelitis. Careful management of fluid intake is necessary and intravenous hydration is probably best avoided. Myocarditis occurs in poliomyelitis. The mild form is probably hypoxic in origin, whereas the severe form may be due to invasion of the heart by the virus. Sterile verrucous endocarditis may occur in poliomyelitis. The problem of the cardiovascular disturbances in poliomyelitis needs further study. Of particular interest is the eventual fate of patients with cardiac abnormalities who survive an attack of this disease.

AUTHORS' SUMMARY.

COCCHI, C. AND PASQUINUCCI, G.: TREATMENT OF TUBERCULOUS MENINGITIS. A SUMMARY OF THREE YEARS' EXPERIENCE AT FLORENCE. (Bulletin World Health Organization, 3:215, 1950).

This study is based on 385 cases of bacteriologically confirmed tuberculous meningitis. Streptomycin formed the basis of treatment and it was found that by giving small intrathecal injections in conjunction with intramuscular injections, it was possible to obtain cures without increasing the intramuscular dosage with its attendant toxic symptoms. The daily intramuscular injection was approximately 10 mg./Kg. of body weight in adults, 20 mg. for children over 2 years of age and 30 mg. for children under 2 years of age. The corresponding daily intrathecal doses were 1 mg., 2 mg., and 3 mg., respectively. In 1949 the intrathecal injections were given twice daily for the first month, once daily for the second and third months and thereafter every other day until the cerebrospinal fluid was normal. An associated dose of 0.1 g./Kg. of body weight per day of a 60 per cent. solution of promin, in 1 or 2 intravenous injections, permitted smaller doses of streptomycin, and drug resistance appeared more slowly during combined therapy. Associated treatment with p-aminosalicylic acid (PAS) was effective in 100 cases. The PAS was given orally (as sodium

salt, 0.3 g./Kg. per day in 3 doses), by intravenous drip (0.5-0.75 g./Kg. per day in terms of free acid for 1-5 months), or intrathecally (as sodium salt, in doses 50-100 mg. for lumbar, 50 mg. for cisternal and ventricular, and 150-200 mg. for subdural routes). Symptoms of intolerance were observed in five per cent. of cases receiving promin but only rarely in those receiving PAS. Treatment was continued until the fluid became normal, generally 6-7 months. In some patients treatment was extended 1-3 months beyond the normalization of the cerebrospinal fluid. Increase in the intensity of the Mantoux, usually accompanied by a return to normal of the erythrocyte sedimentation rate, often preceded attainment of fluid normality. There was an evident relation between streptomycin resistance and mortality, and between appearance of resistance and duration of therapy. It was found that patients, who had relapses and from whom streptomycin-resistant organisms were isolated, responded well to treatment with PAS and streptomycin. Of 267 patients, 147 have survived and 129 have normal cerebrospinal fluid. The general condition of the cured patients is very good. In only 14 of them have sequelae persisted.

MICHAEL A. BRESCIA, M.D.

CAMPBELL, W. A. B.; CHEESEMAN, E. A. AND KILPATRICK, A.: THE EFFECTS OF NEONATAL ASPHYXIA ON PHYSICAL AND MENTAL DEVELOPMENT. (Archives of Disease in Childhood, 25: 351, Dec. 1950).

The authors studied 267 children as to mental and physical development 89 of whom had asphyxia neonatorum and 178 of whom were unselected controls. No significant difference was found in the average physical measurements (height, weight, inspired chest measurement and chest expansion) or in hemoglobin levels or in intelligence distributions (as assessed from Raven's matrices) between the "asphyxia" and the control group. The exception occurred in the comparison of the mean chest measurements of first born males: the mean for the "asphyxia" group was just significantly less than that for the control group. Contrary to the general impression, the present data and analysis give no support for the hypothesis that asphyxia neonatorum is a common cause of later mental and physical retardation.

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